

Human Neocortical Neurosolver

A New Tool for Circuit Level Interpretation of MEG/EEG Signals



Stephanie R. Jones
Brown University, Department of Neuroscience
Providence VA, Center for Neurorestoration and Neurotechnology

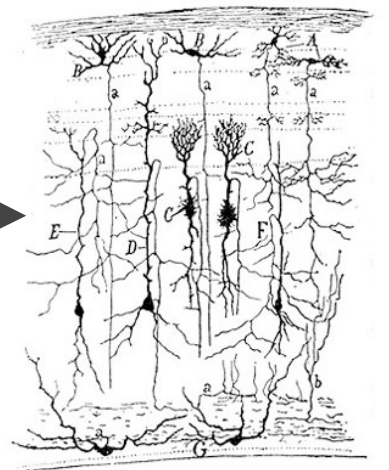
Challenge in Human Neuroscience: Connect Macroscale Human MEG/EEG Signals to Cellular and Circuit Level Electrophysiology

Human Non-Invasive
Electrophysiology



?

Electrophysiological
Measurements



Extracranially Measured
Macroscale Signals

Cellular & Circuit
Level Dynamics

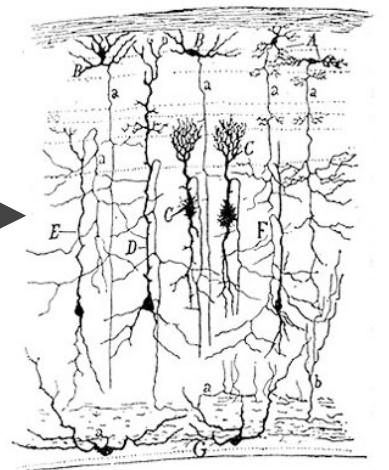
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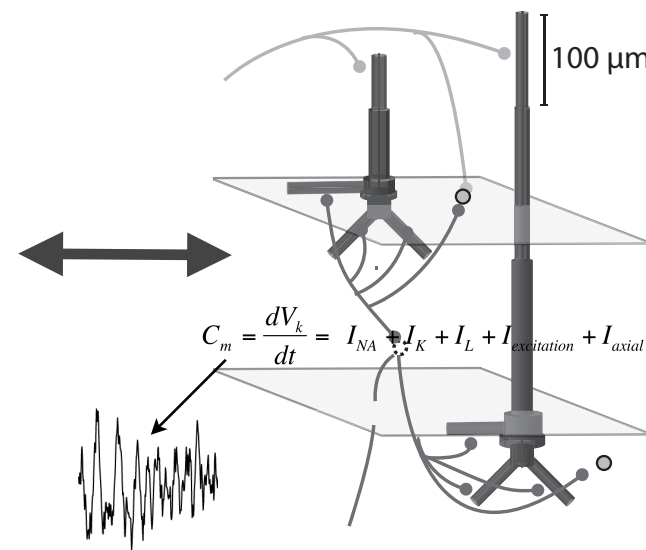
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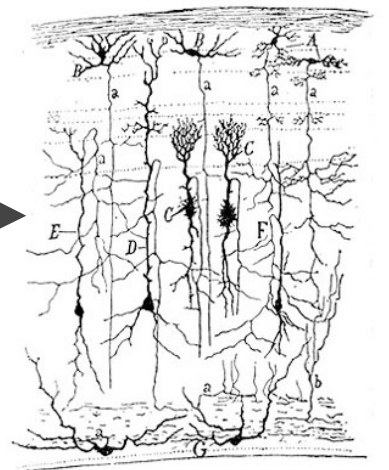
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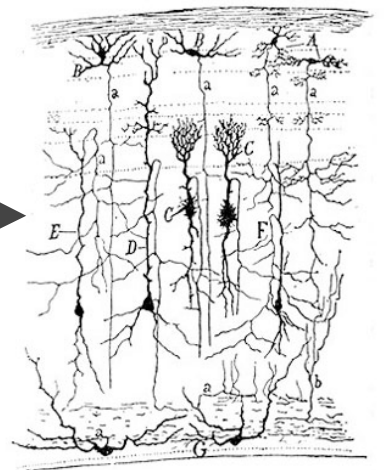
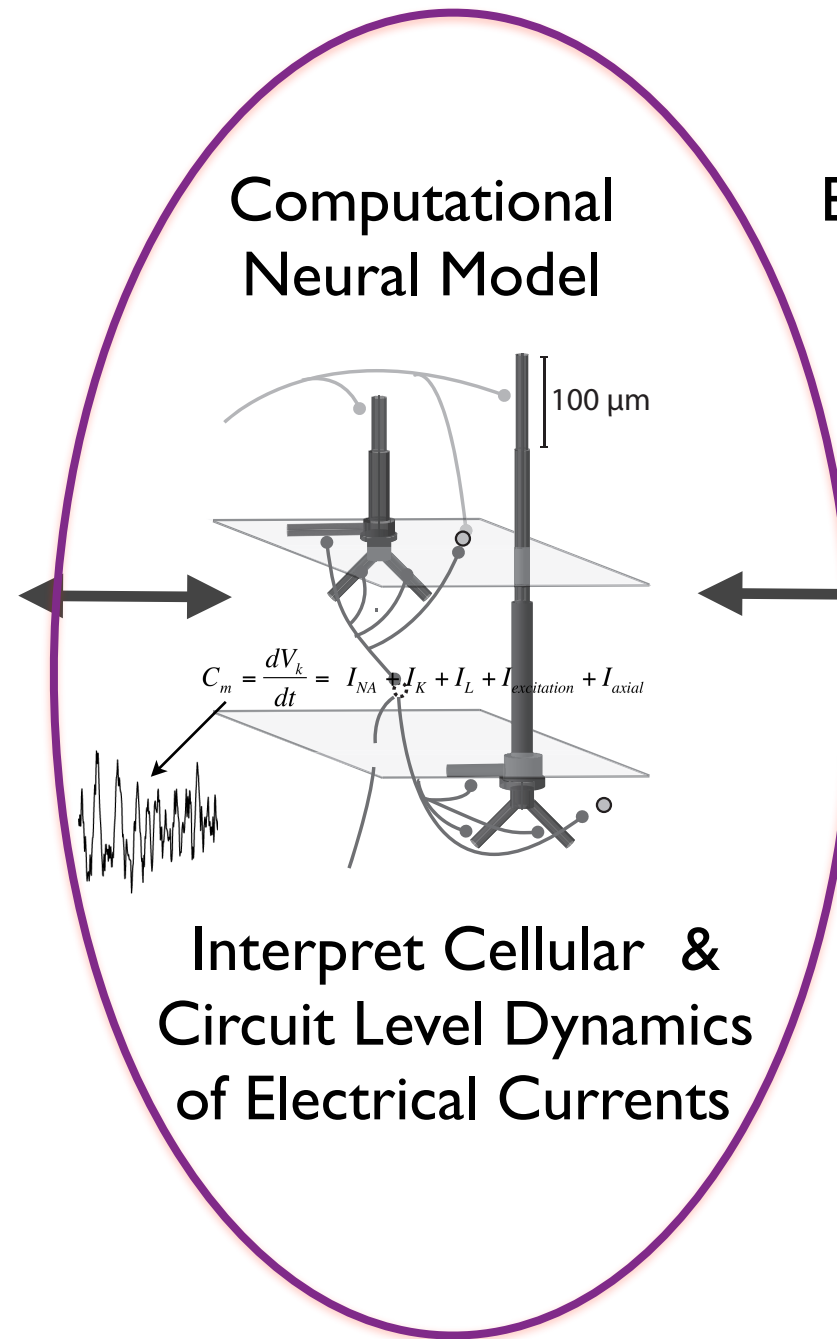
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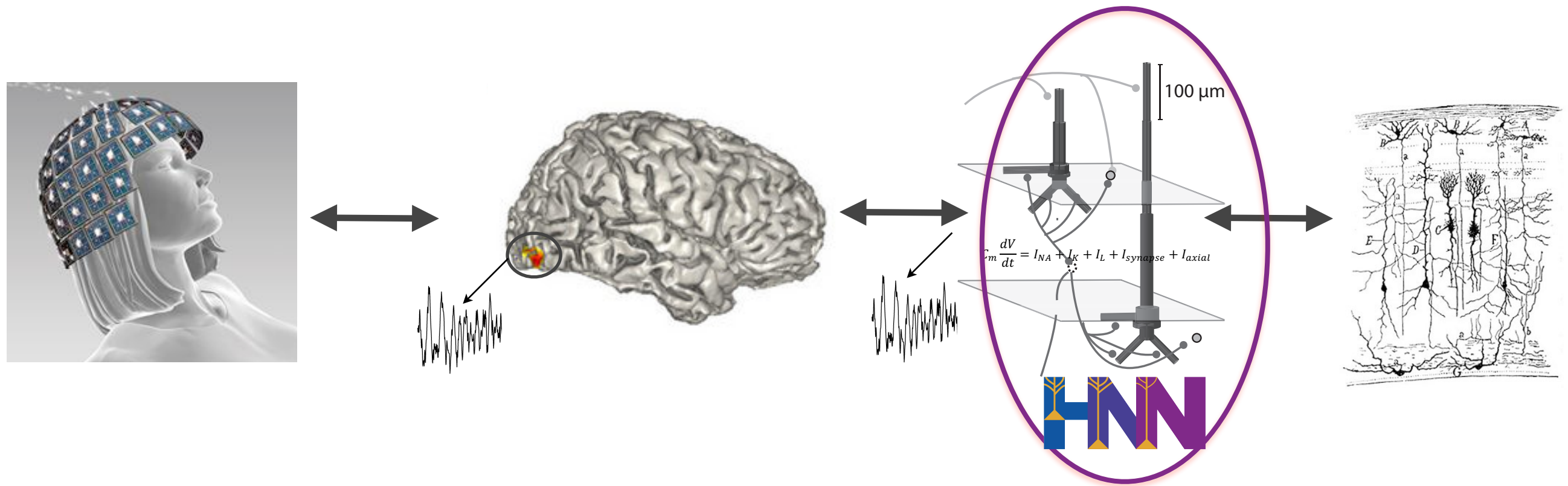


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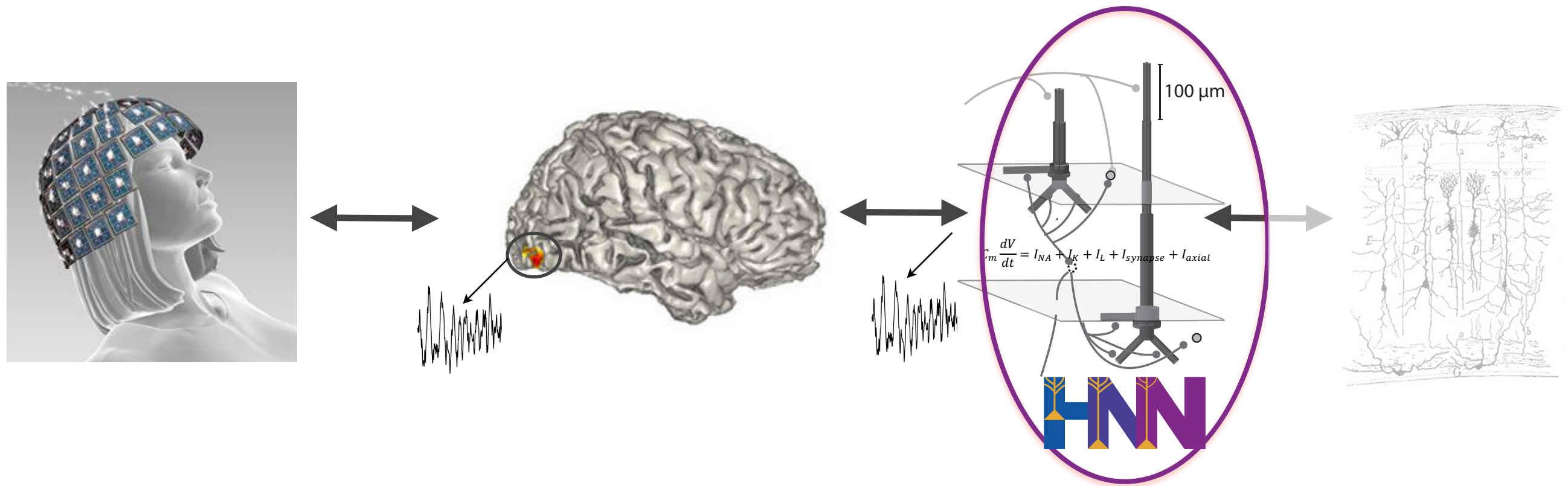


Human Neocortical Neurosolver



Talk Outline

- A new computational neural modeling tool for circuit level investigation of human EEG/MEG signals generation: Human Neocortical Neurosolver (HNN)
- HNN reveals novel mechanisms and meaning of brain rhythms and sensory evoked responses
- A brief tour of HNN: GUI driven, open-source access, tutorials



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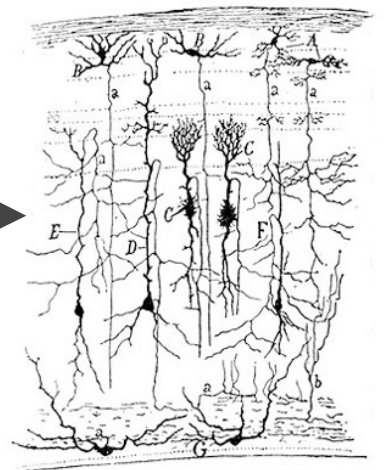
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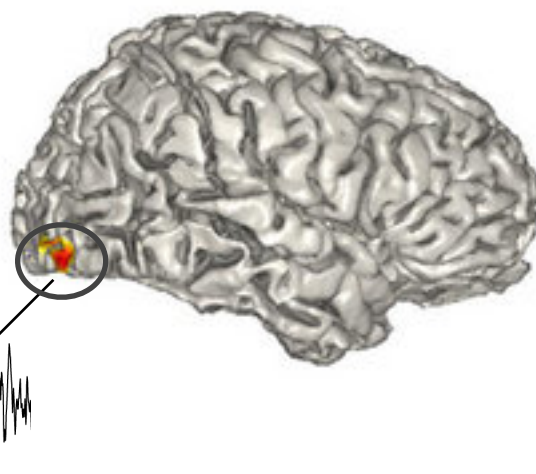
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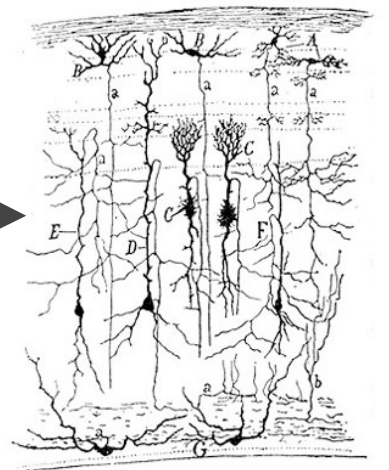
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Current Source
Estimation Model



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Estimate Locations
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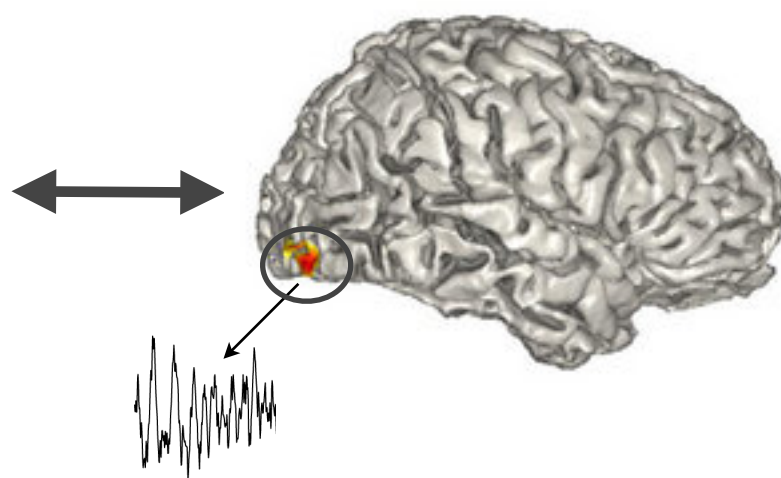
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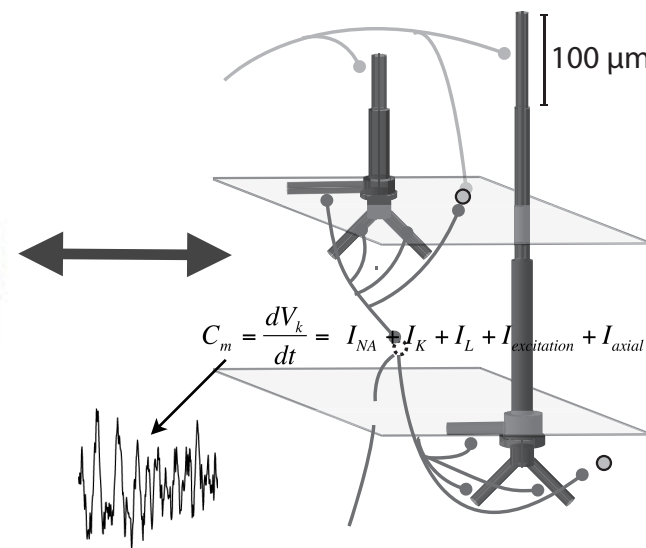
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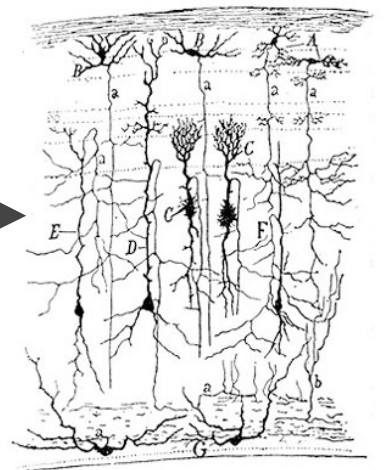
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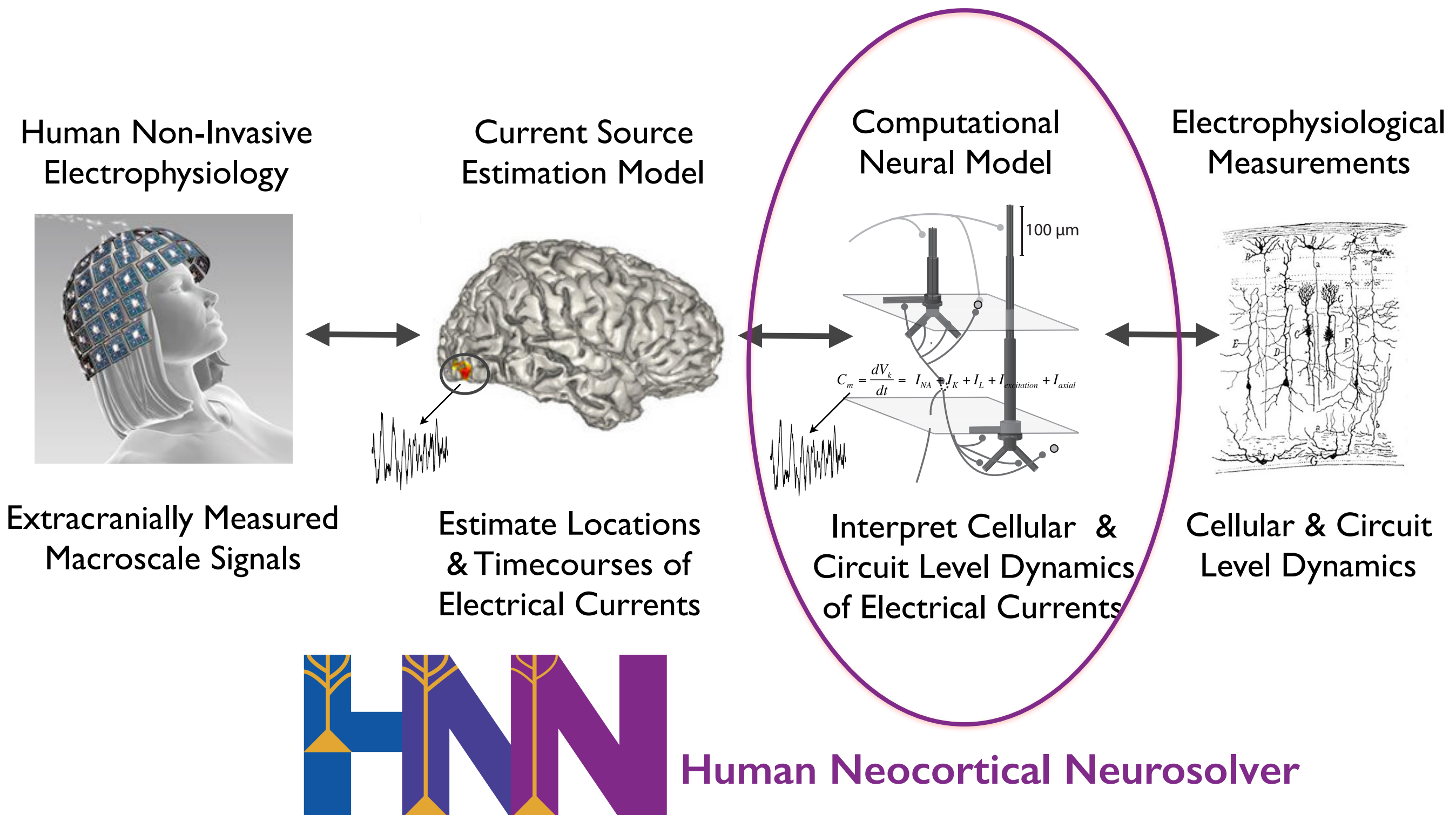
Interpret Cellular &
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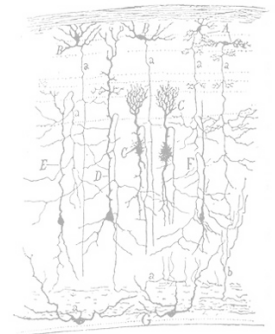
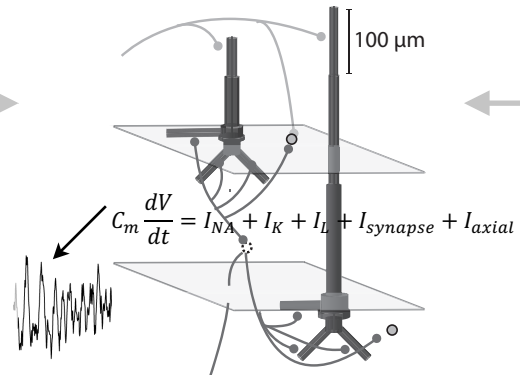
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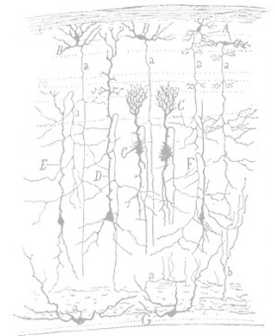
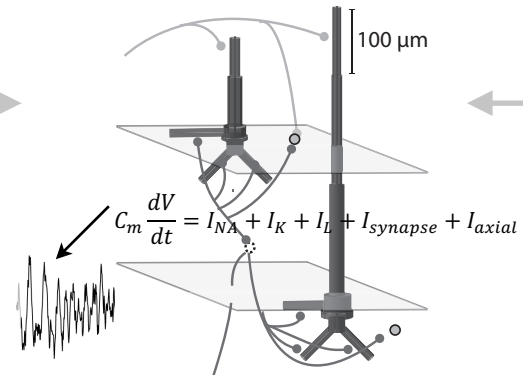


Modeling Human Neural Dynamics

$$\frac{dX}{dt} = \sum Y_j$$

$$\frac{dY_j}{dt} = f_j(t)$$

A system of differential equations that describe how electrical activity created by neurons changes over time



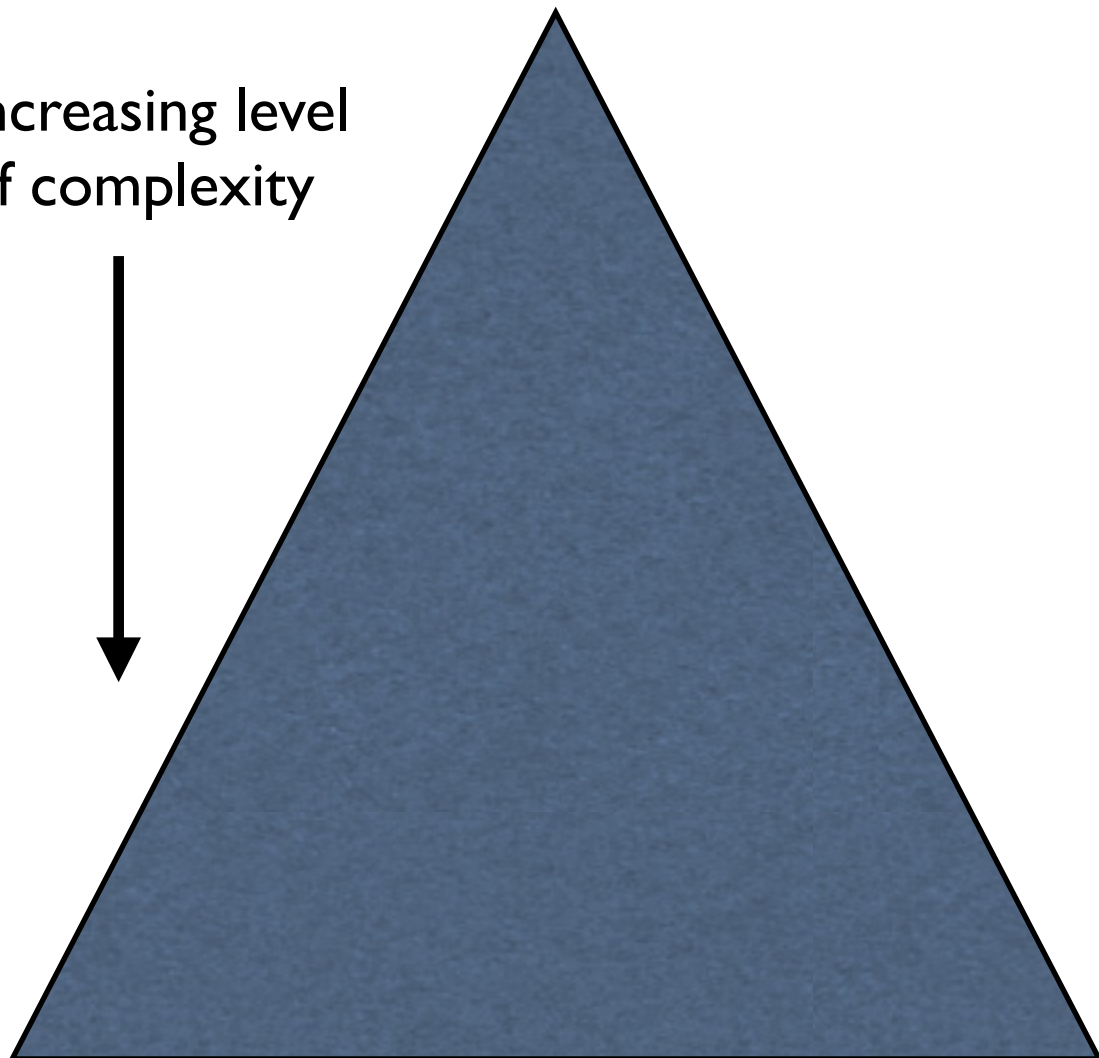
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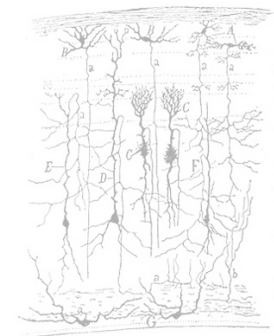
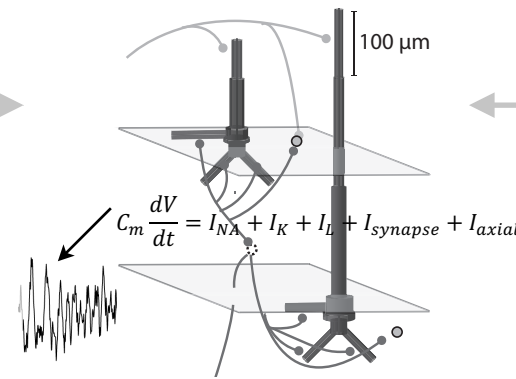
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Increasing level
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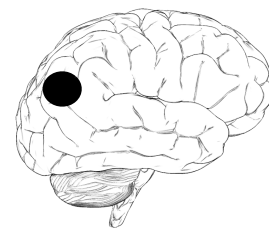
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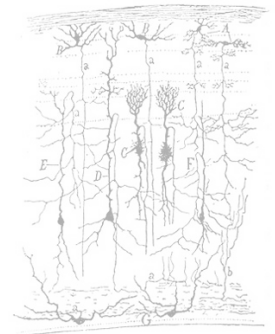
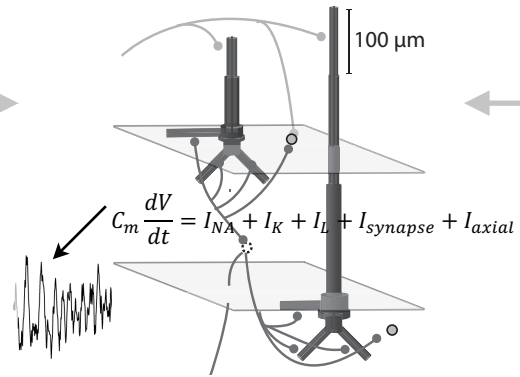
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Increasing level of complexity



Population Models (Neural Mass Models); small number of variables represent the mean “state” of a large populations of neurons



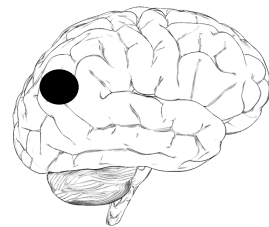
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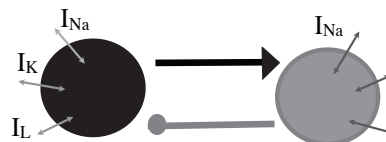
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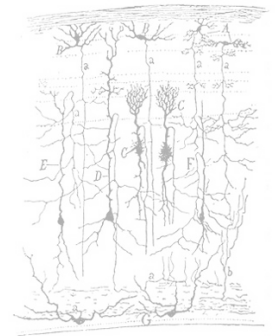
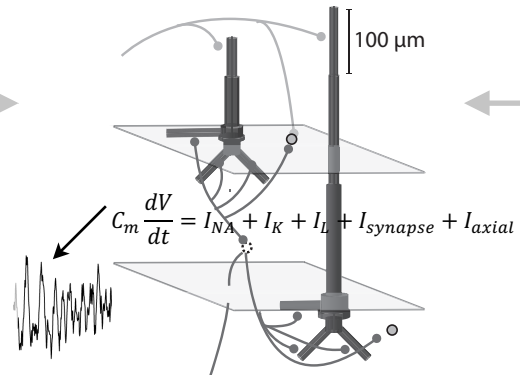
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Individual spiking neurons modeled
and connected in reduced forms



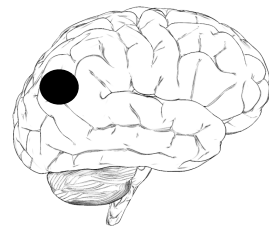
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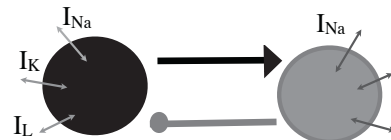
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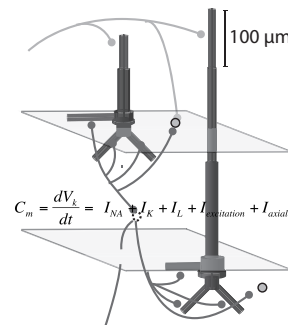
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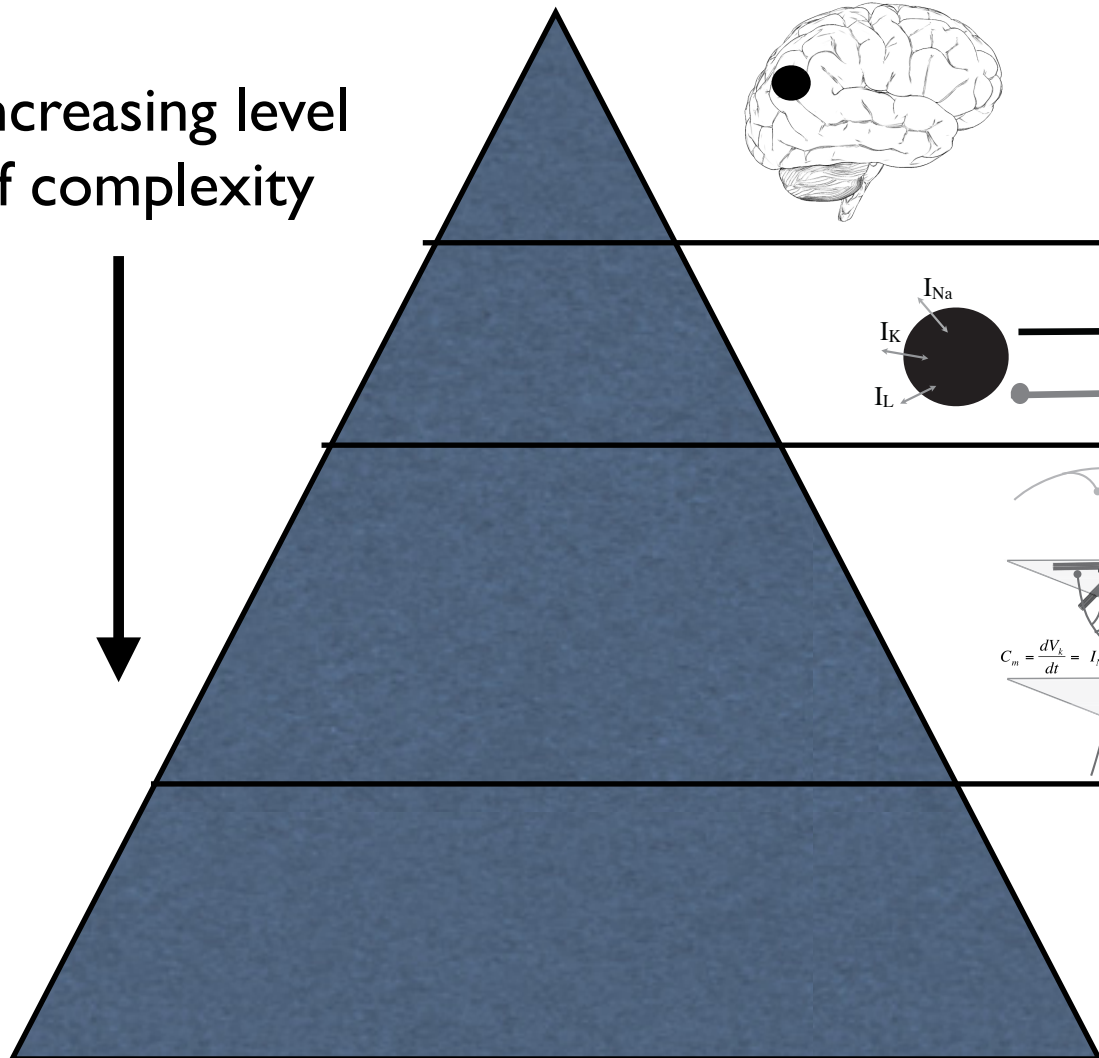
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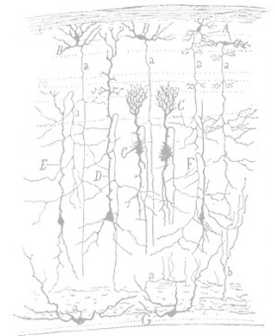
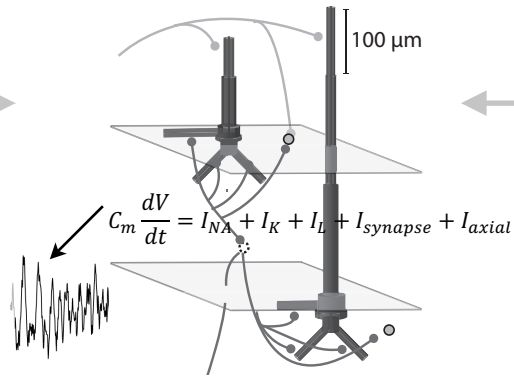


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Inclusion of anatomy and physiology of
individual neurons, laminar structure,
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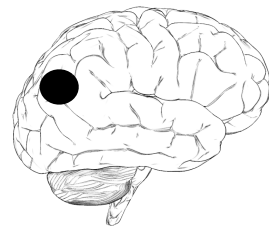
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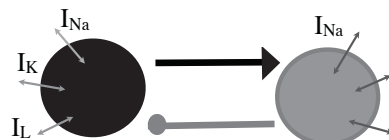
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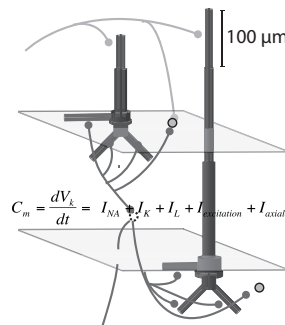
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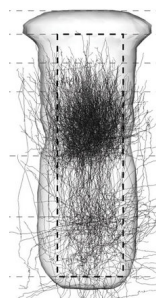
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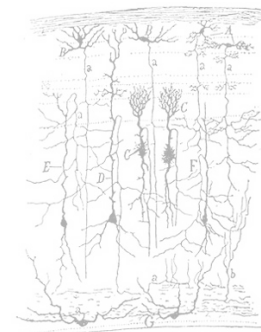
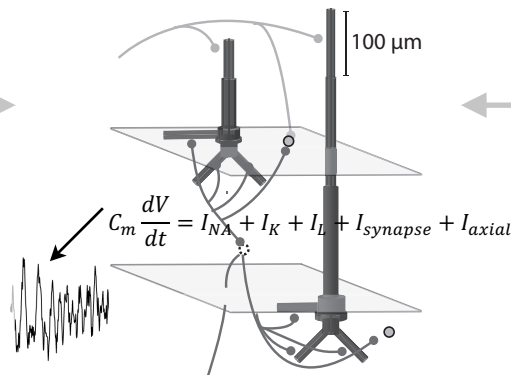
Individual spiking neurons modeled and connected in reduced forms



Inclusion of anatomy and physiology of individual neurons, laminar structure, and network connectivity



Detailed anatomy and physiology of all neurons, laminar structure, and network connectivity



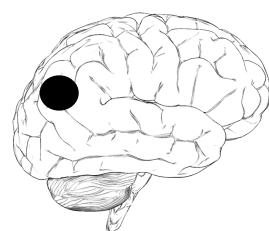
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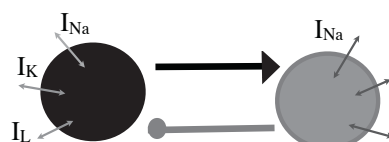
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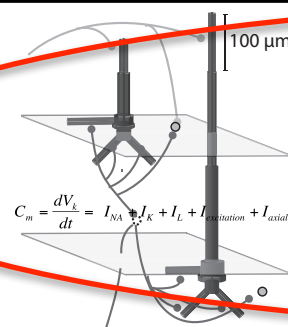
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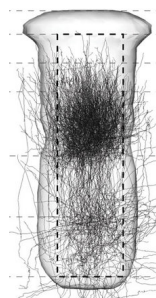
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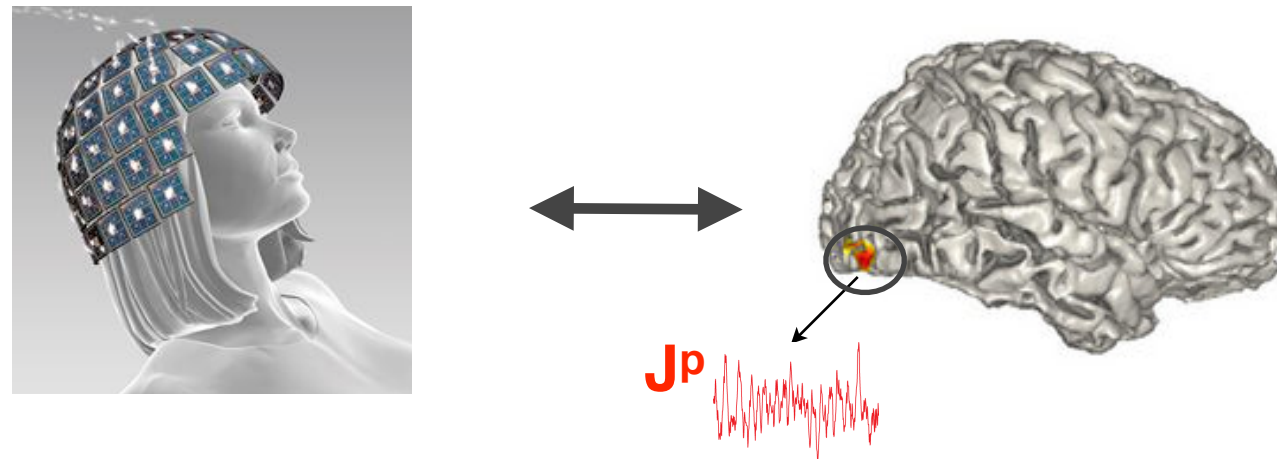
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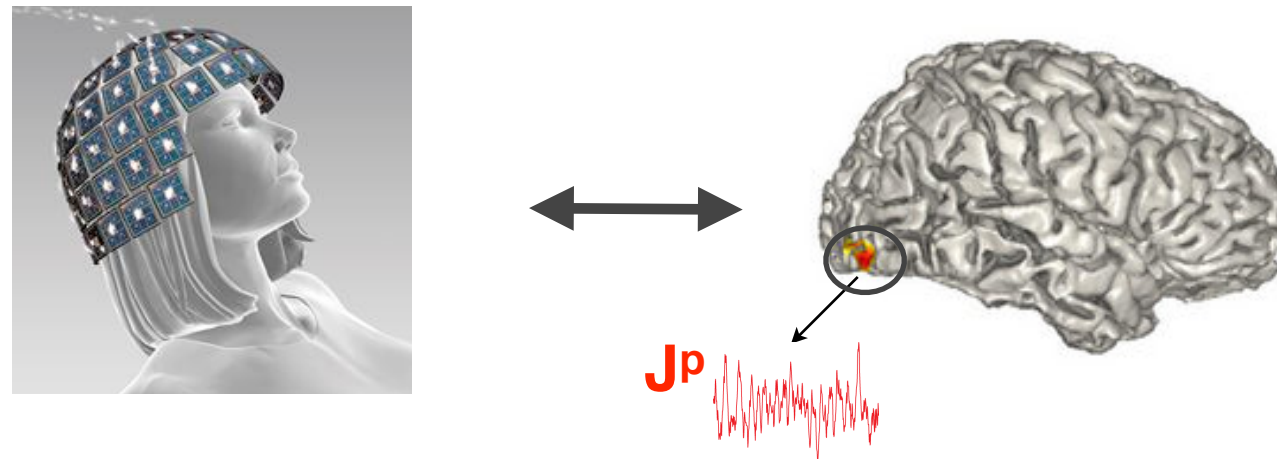
Connecting MEG/EEG Recordings to Circuit Level Details

1. Inverse solution methods estimate the location, direction, time course of the primary electrical currents ($\mathbf{J_p}$) that create the recorded sensor data

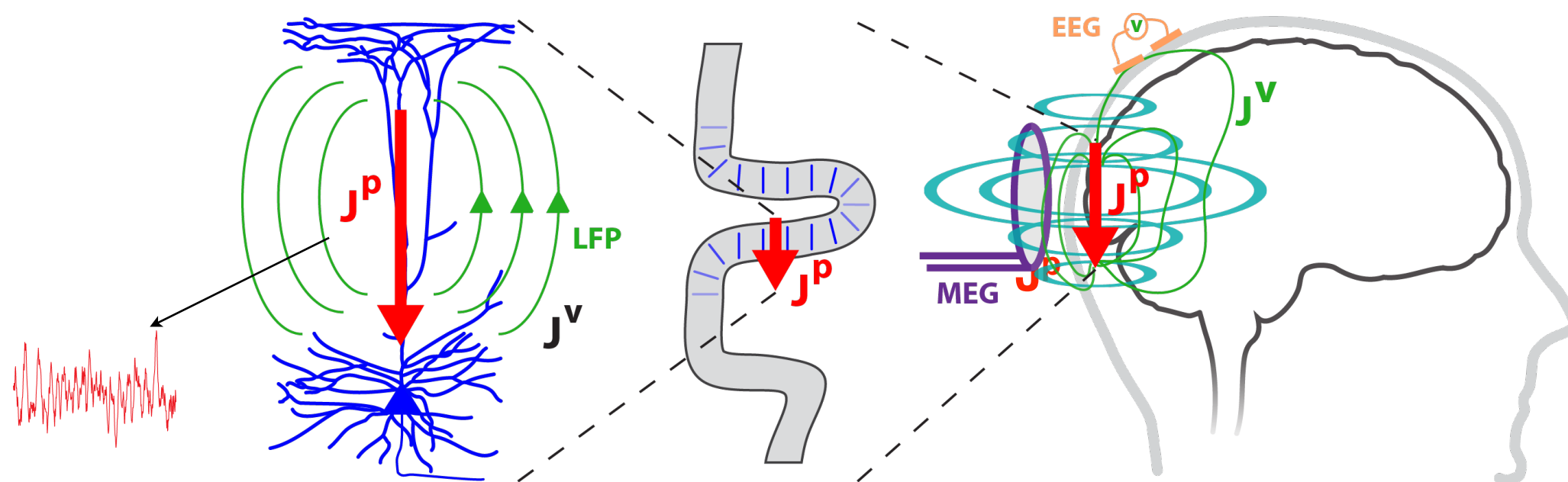


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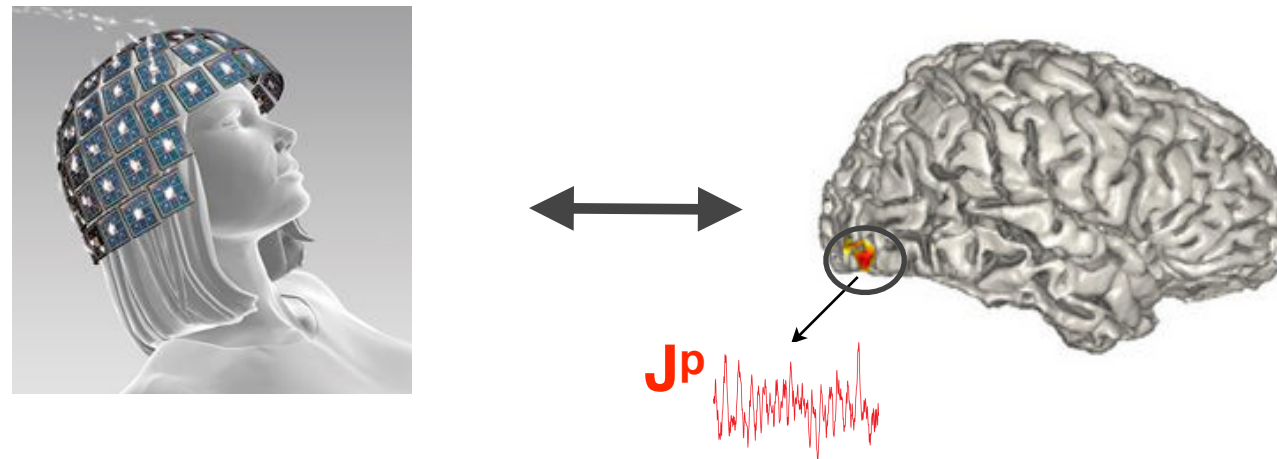


2. The primary currents are generated by the post-synaptic intracellular current flow in long and spatially aligned cortical pyramidal neuron dendrites

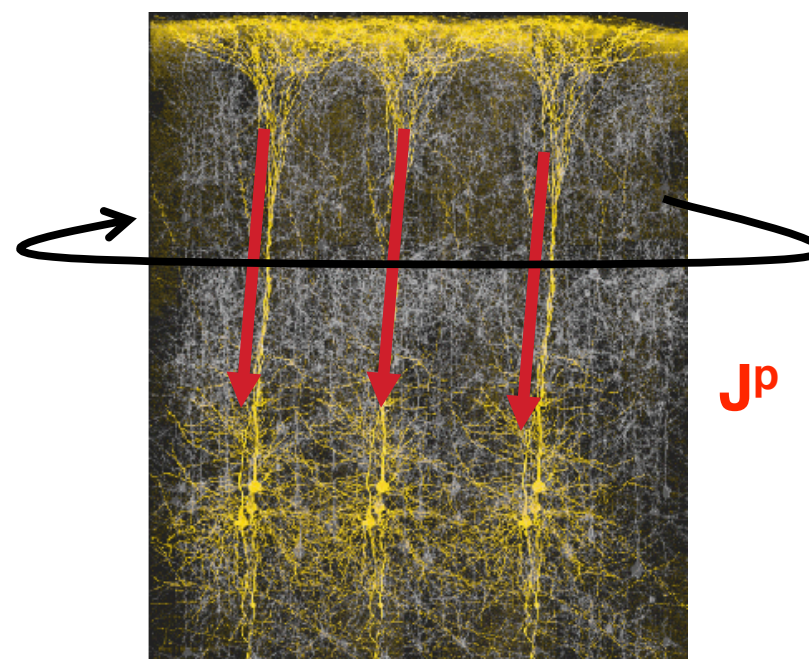


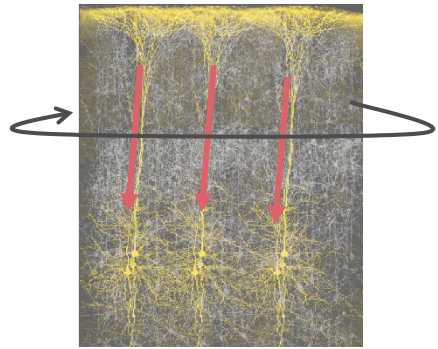
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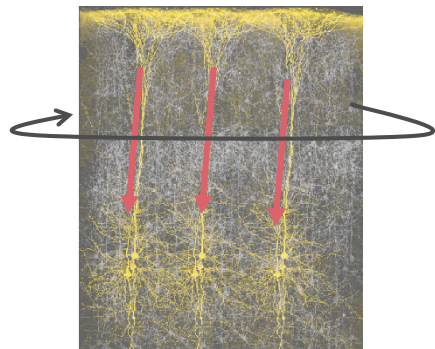


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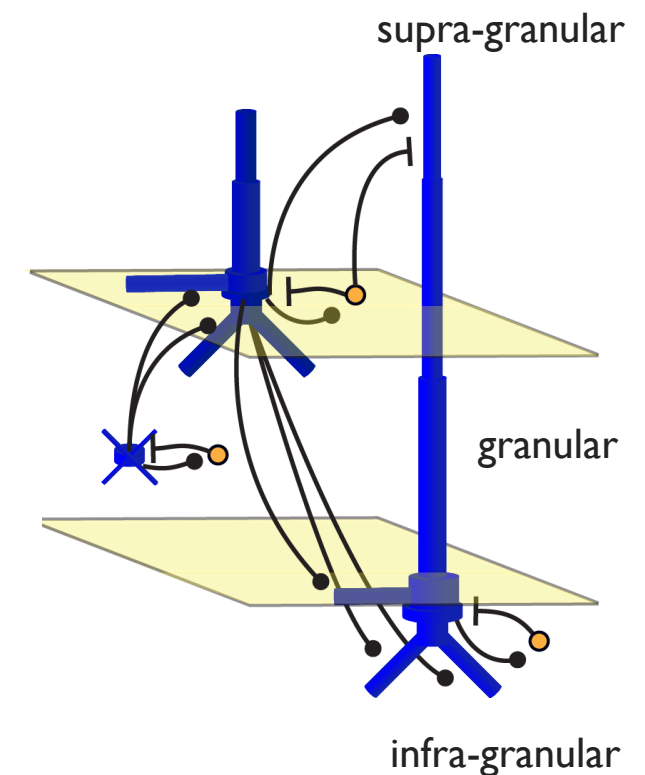


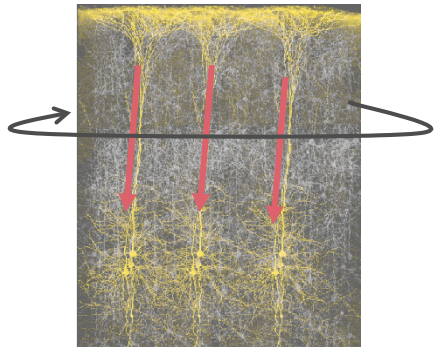
Key Canonical Cortical Circuitry Features that Contributes to Macroscale Signal



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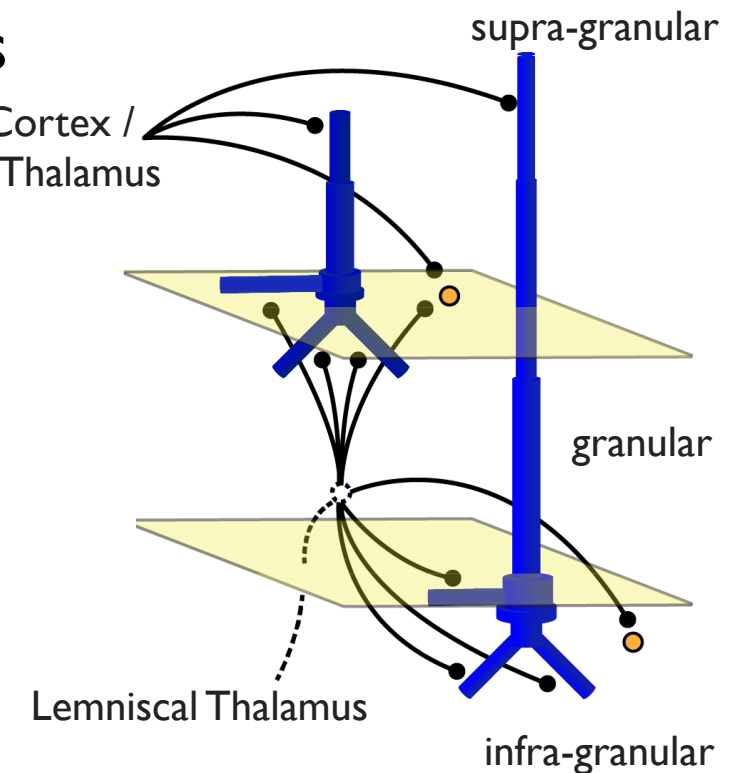
- Layered structure with excitatory and inhibitory interactions

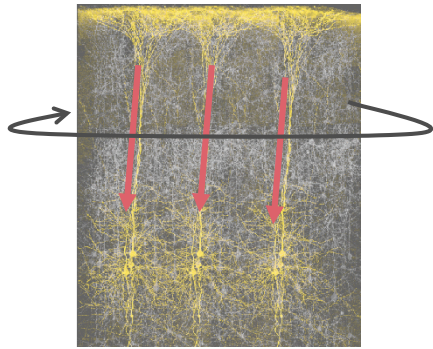




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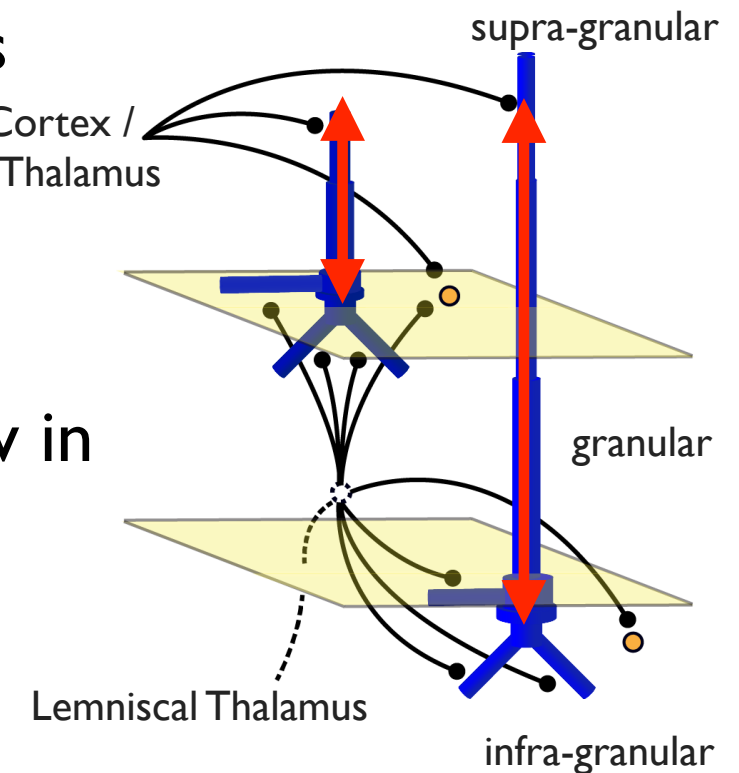
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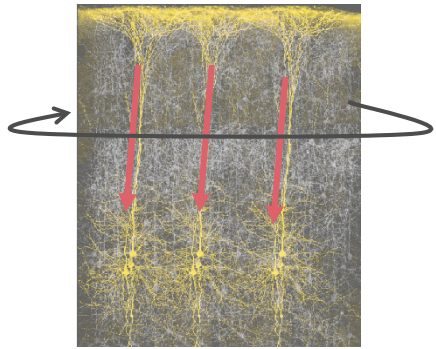




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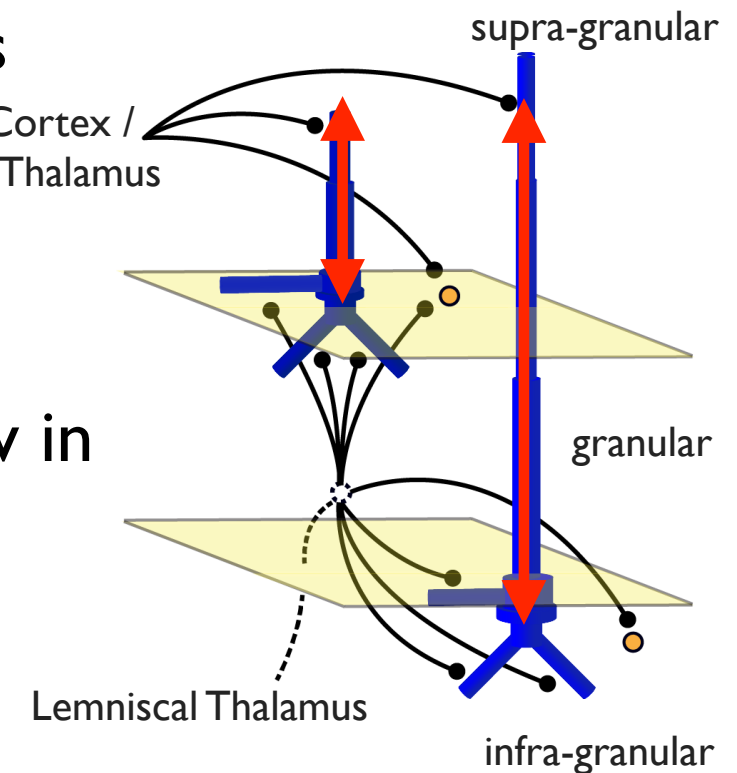
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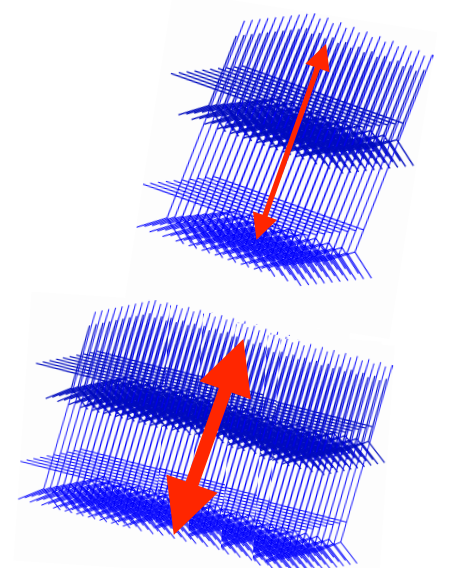
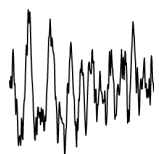
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- ERPs typically 10-100nAm. ~10,000 synchronously firing PN



- Low frequency rhythms 100-1000nAm. ~1,000,000 subthreshold PN



Canonical Layered Cortical Circuit Model to Simulate Macroscale Dynamics with Circuit Details

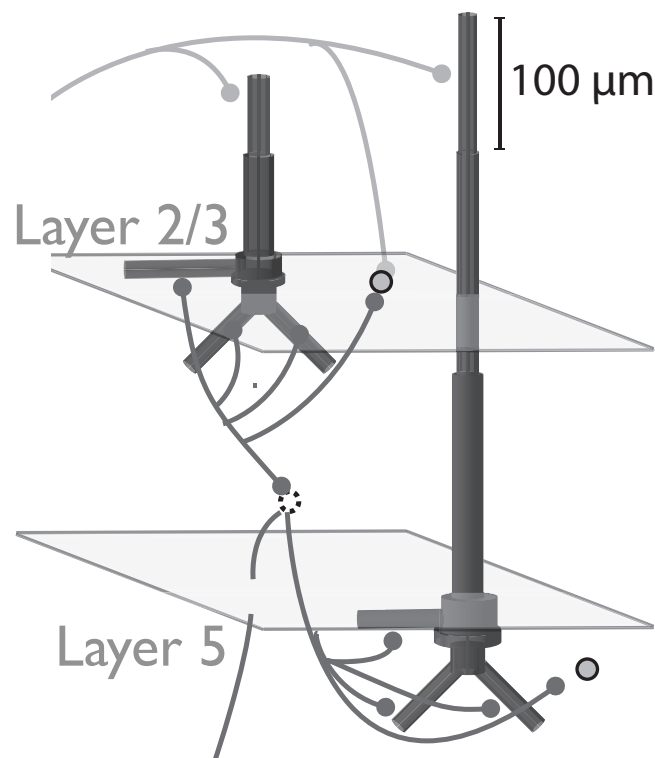
Local Network

- Multi-Compartment Pyramidal Neurons (PN)
- Single Compartment Inhibitory Neurons
- Gabaergic & Glutamatergic Synapses
- Hodgkin-Huxley Dynamics

$$C_m \frac{dV_k}{dt} = I_{NA} + I_K + I_L + I_{synapse} + I_{axial}$$

Multi-Compartment Cell
 k = compartment

Rall's Cable
Equations



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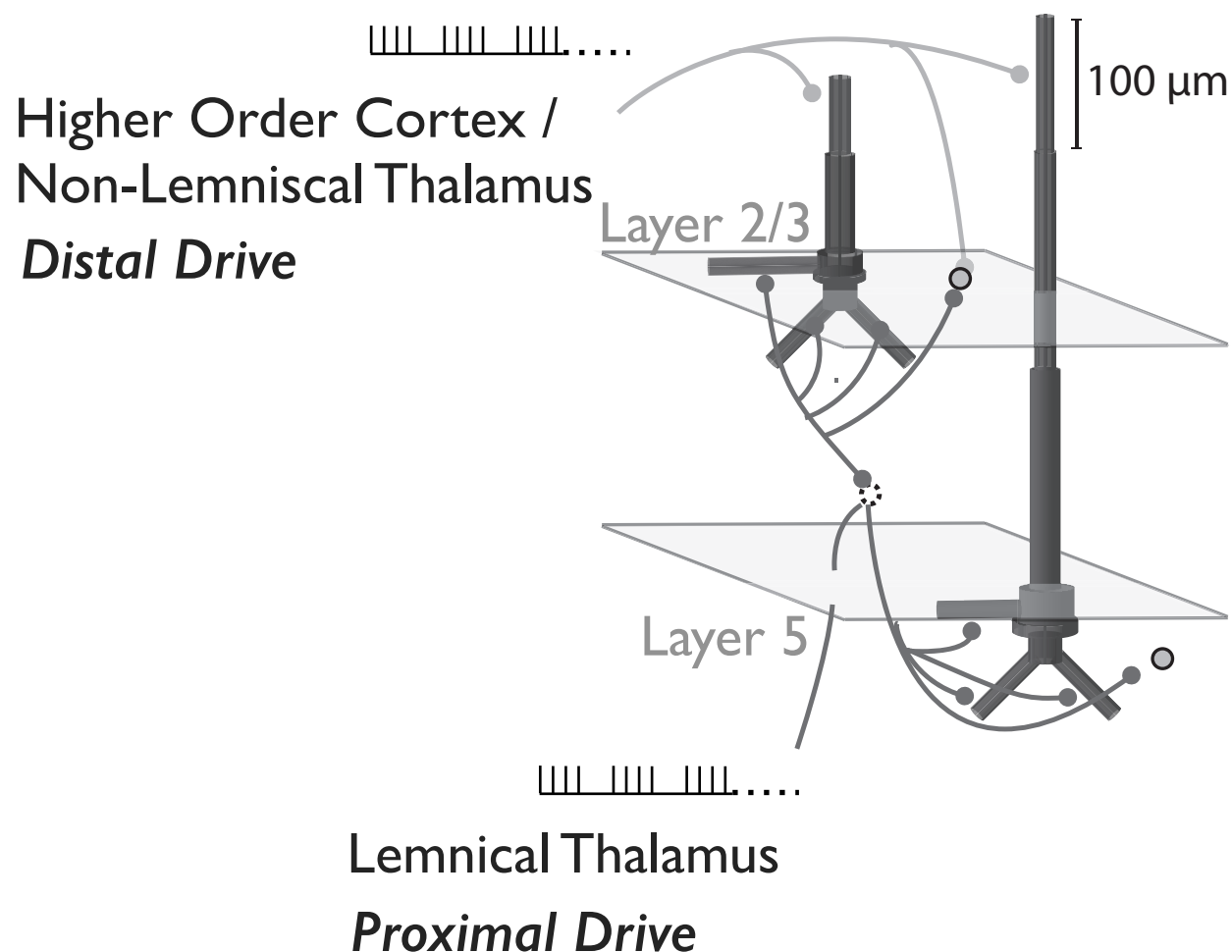
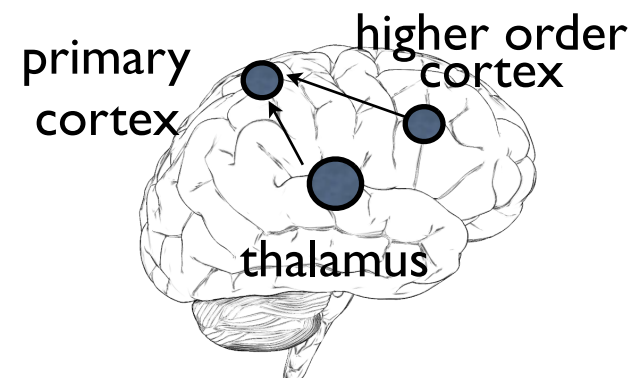
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Exogenous Drive

- Layer Specific Synaptic Drive
 (Proximal and Distal)



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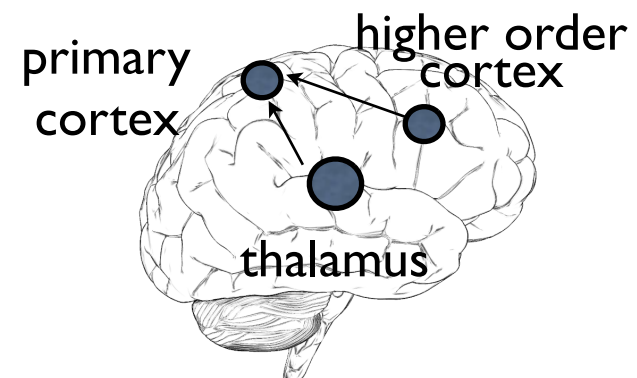
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Rall's Cable Equations

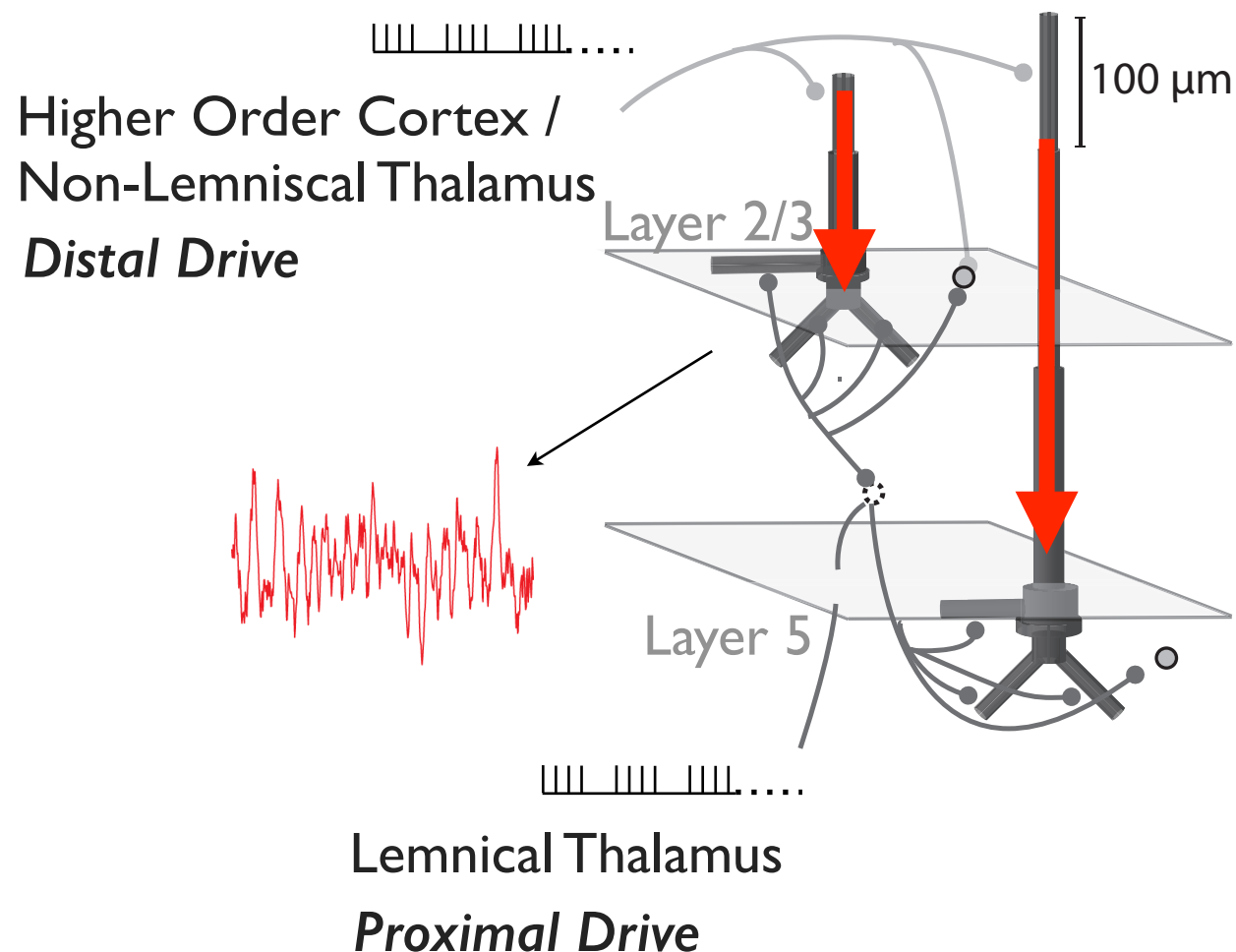
Exogenous Drive

- Layer Specific Synaptic Drive (Proximal and Distal)



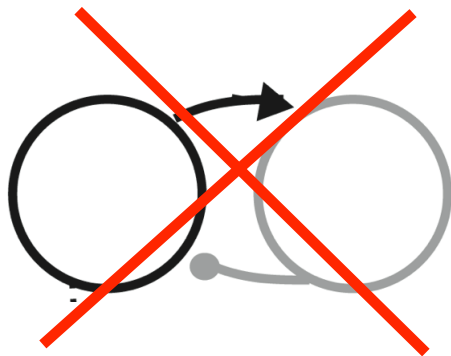
Primary Current Calculation

- **Primary Current Dipole:** Net Intracellular Current Flow in PN dendrites
- Units: nano-Ampere-meters (nAm)



Canonical Layered Cortical Circuit Model to Simulate Macroscale Dynamics with Circuit Details

Simplified
Models



Do not account for
biophysics of the signal!

Local Network

- Multi-Compartment Pyramidal Neurons (PN)
- Single Compartment Inhibitory Neurons
- Gabaergic & Glutamatergic Synapses
- Hodgkin-Huxley Dynamics

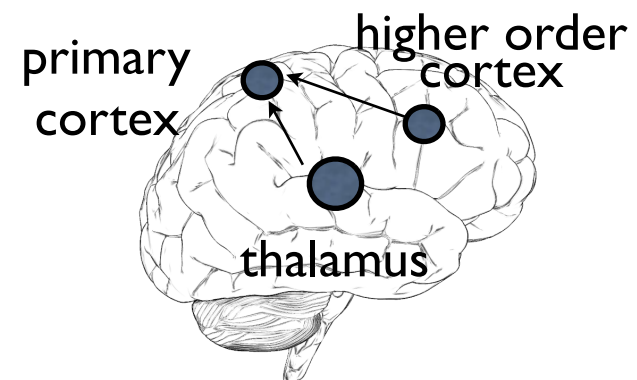
$$C_m \frac{dV_k}{dt} = I_{NA} + I_K + I_L + I_{synapse} + I_{axial}$$

Multi-Compartment Cell
 k = compartment

Rall's Cable
Equations

Exogenous Drive

- Layer Specific Synaptic Drive
(Proximal and Distal)



Primary Current Calculation

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Canonical Layered Cortical Circuit Model to Simulate Macroscale Dynamics with Circuit Details

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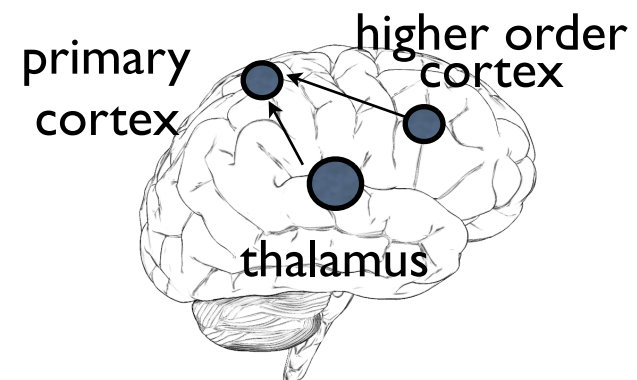
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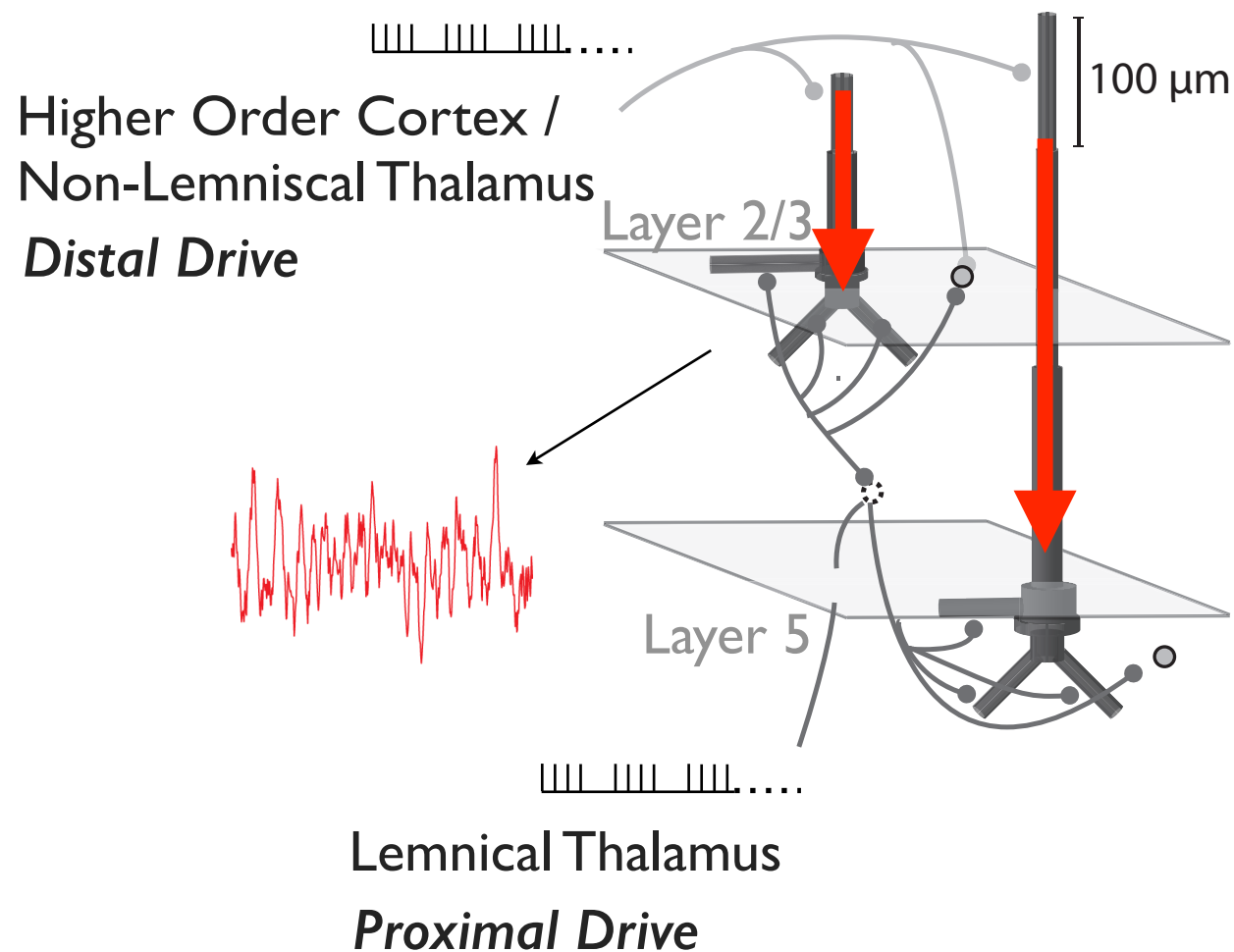
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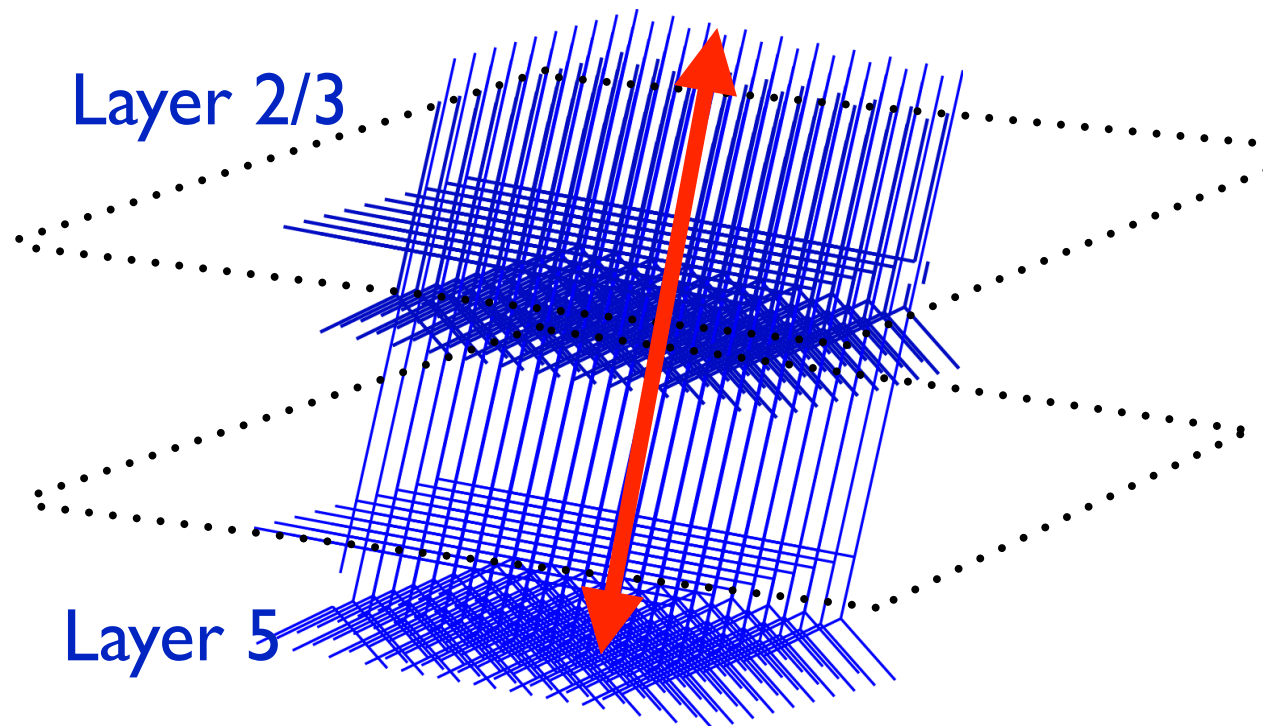


Human Neocortical Neurosolver

A new tool for circuit level interpretation of MEG/EEG



Cortical Column

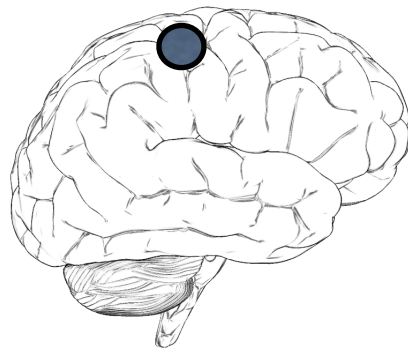


100-1000s pyramidal neurons & 1/3
ratio of inhibitory neurons per layer'

- Unique model of **human current source signals** from dendritic current flow.
- User-friendly, GUI driven, hypothesis development and testing tool.
<http://hnn.brown.edu>
- In collaboration with Matti Hämäläinen, integrating with current source modeling (minimum-norm-estimation).
<http://martinos.org/mne/stable/index.html>
<http://mmvt.org> (Noam Peled)

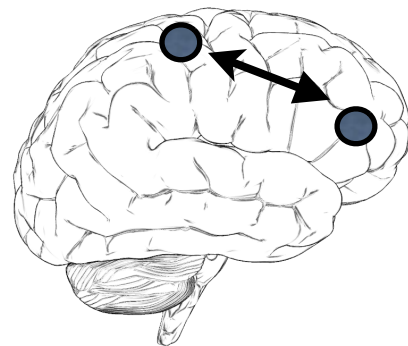
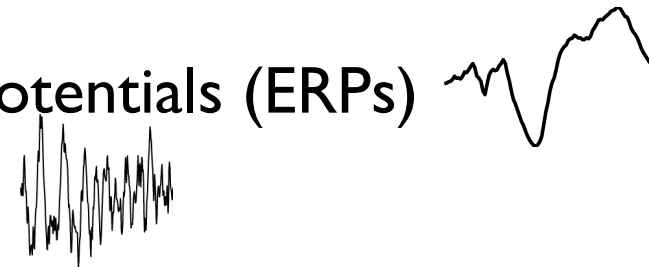
Potential MEG/EEG Signals to Study with HNN

Increasing level
of complexity

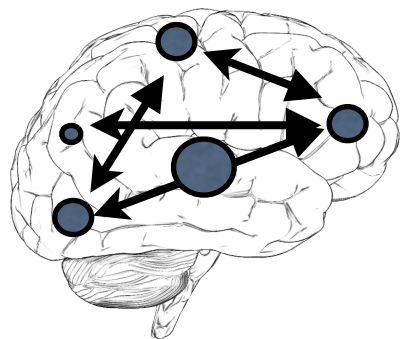


Event Related Potentials (ERPs)

Brain Rhythms



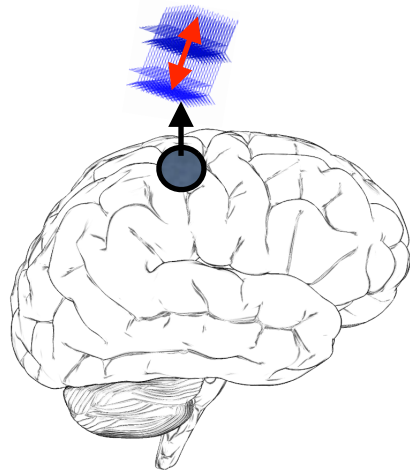
Inter-Area Functional Connectivity (e.g. power or phase-coherence, cross-frequency coupling, microstates)



Machine Learning Algorithms, Graph Theoretical Measures to Classify Network States

Potential MEG/EEG Signals to Study with HNN

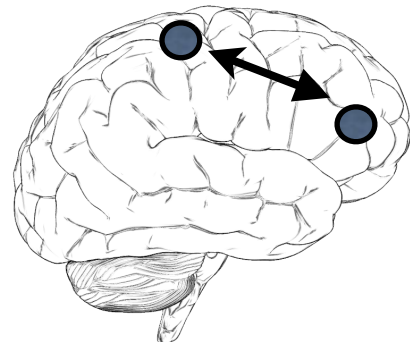
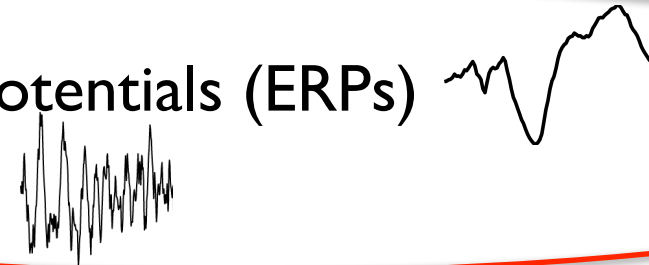
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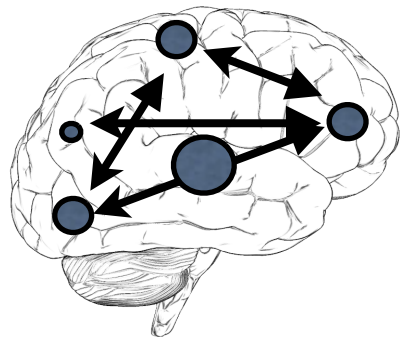
Lowest Hanging Fruit to Connect to Microcircuit Details

Event Related Potentials (ERPs)

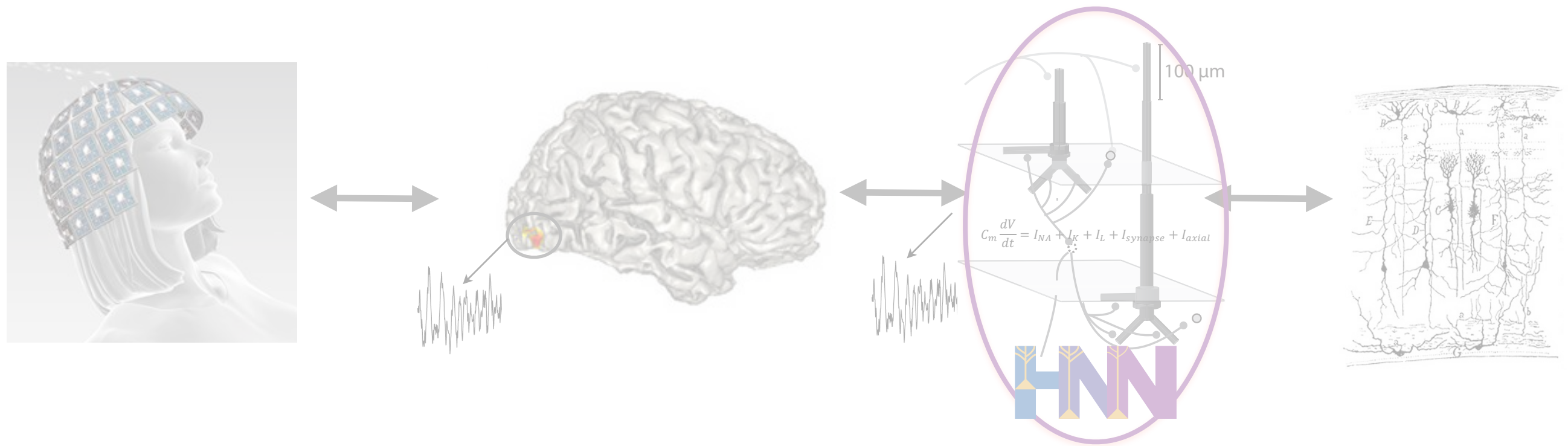
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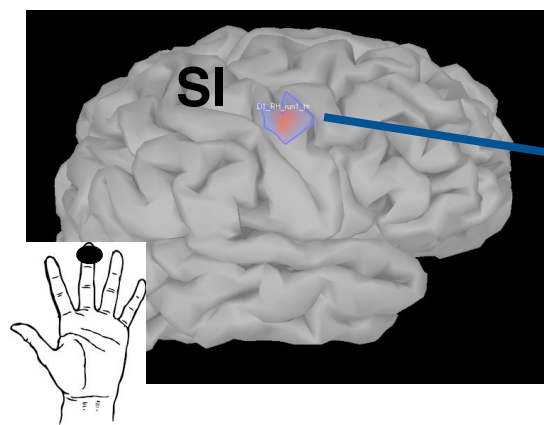
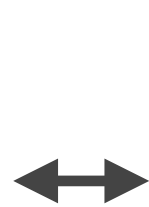
Machine Learning Algorithms, Graph Theoretical Measures to Classify Network States



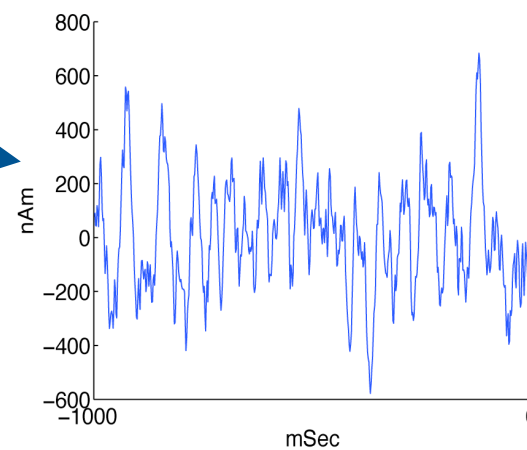
Talk Outline

- Human Neocortical Neurosolver (HNN): A computational neural modeling tool for circuit level investigation of MEG/EEG signals generation
- HNN reveals novel mechanisms and meaning of brain rhythms and sensory evoked responses
- A brief tour of HNN: GUI driven, open-source access, tutorials

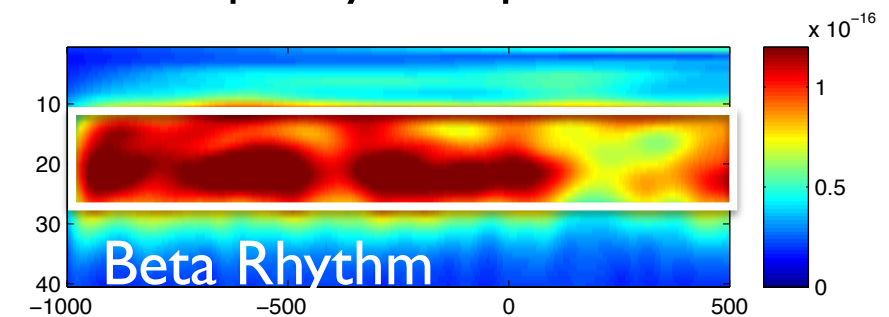
Beta (15-29Hz) is a Prominent Low Frequency Somatosensory Rhythm



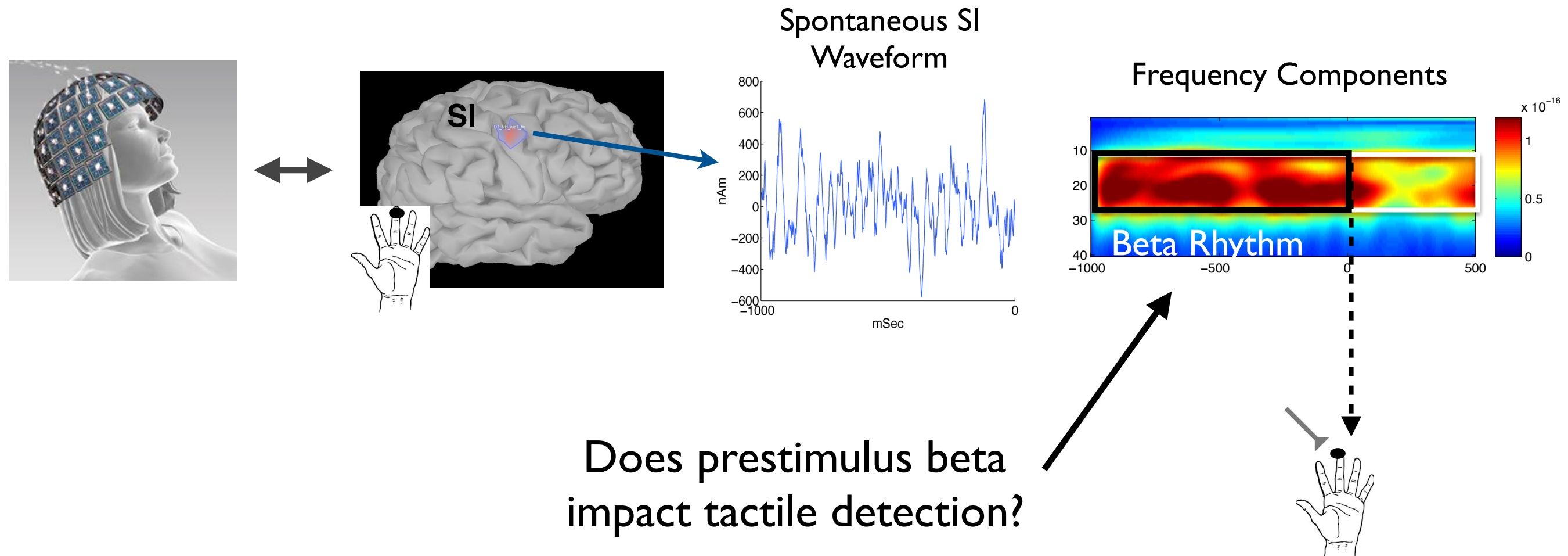
Spontaneous SI
Waveform



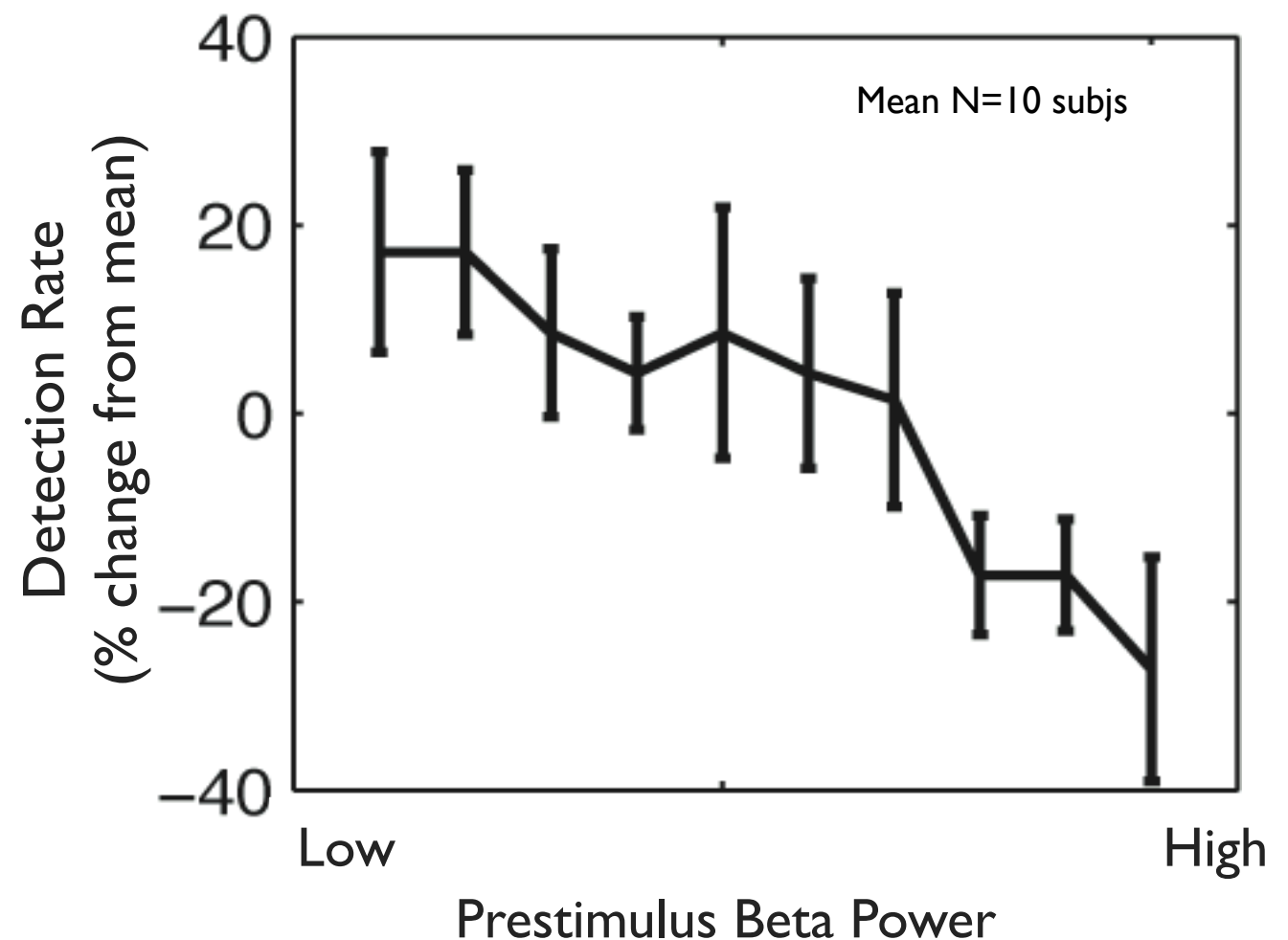
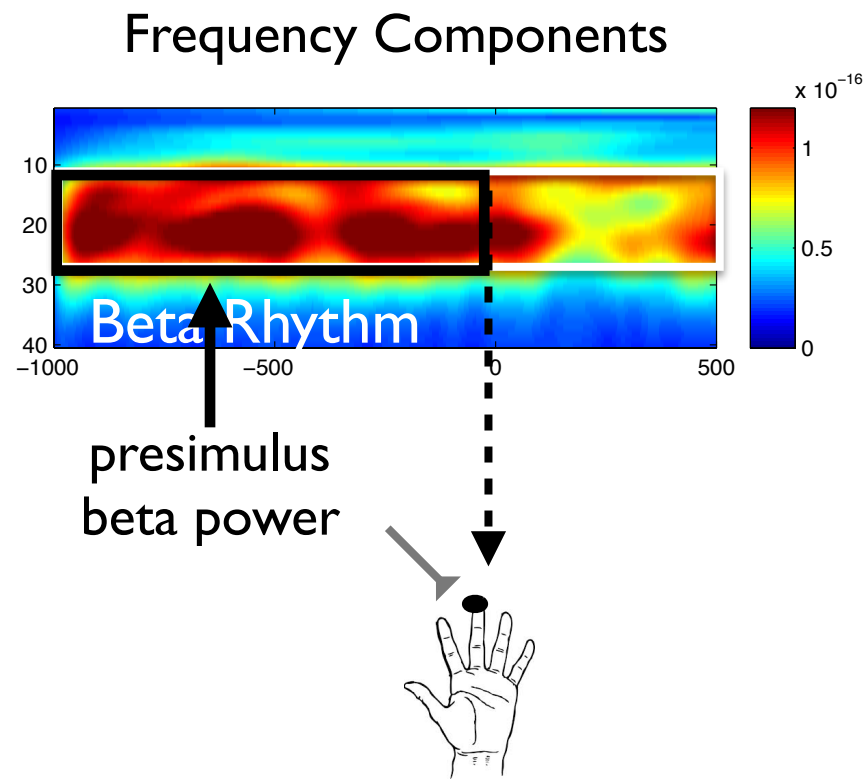
Frequency Components



Beta (15-29Hz) is a Prominent Low Frequency Somatosensory Rhythm



Beta Rhythms (15-29Hz) Decrease the Salience of Sensory Signals

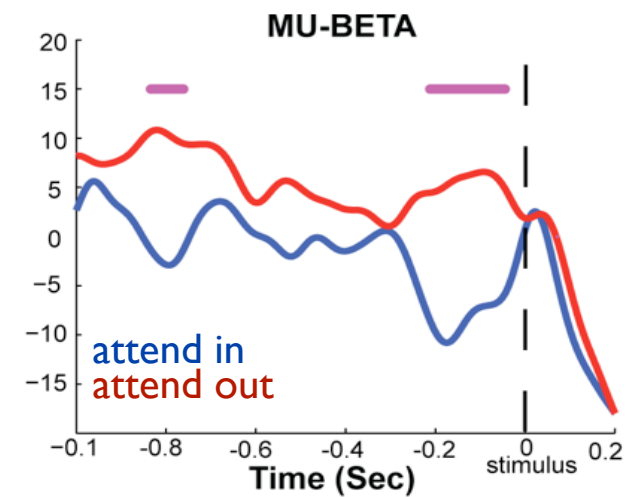
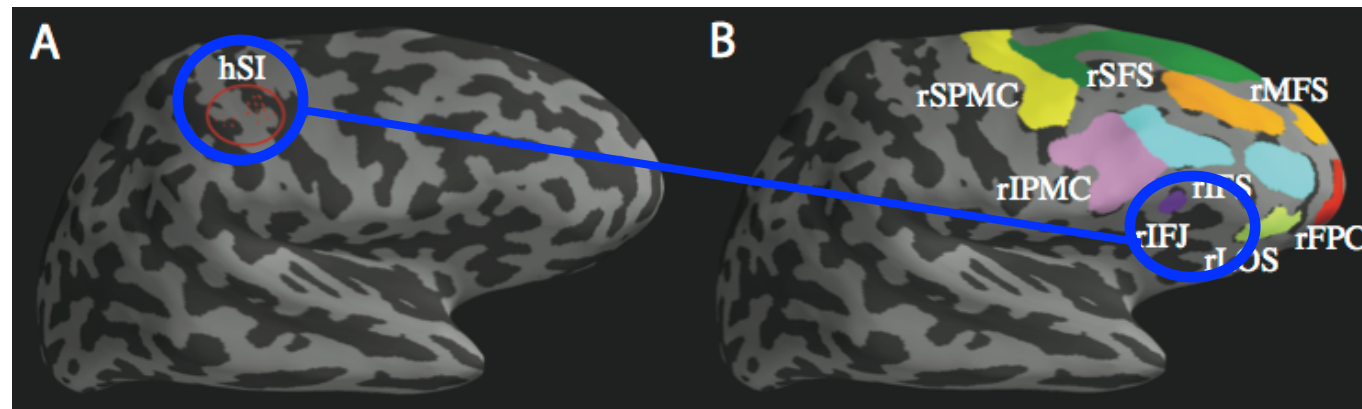
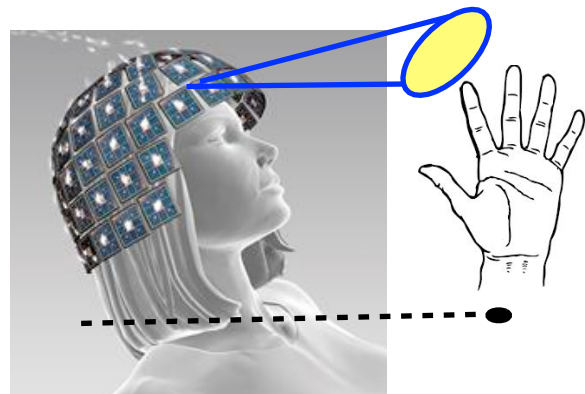


High beta power is a signature of “inhibited” perception

Prestimulus Beta “Inhibits” Processing

- Beta power and inter-area coherence decrease with cued attention.

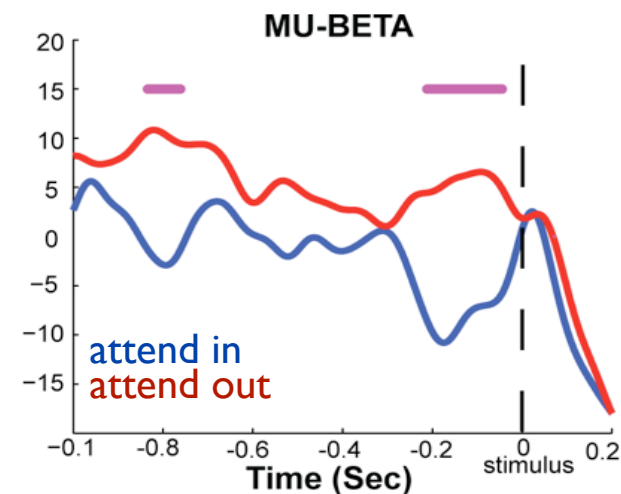
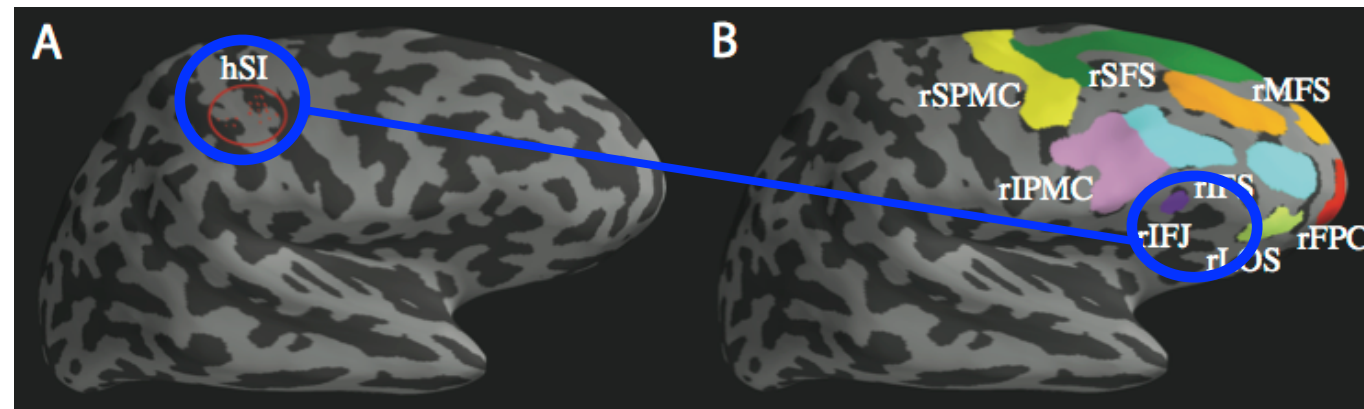
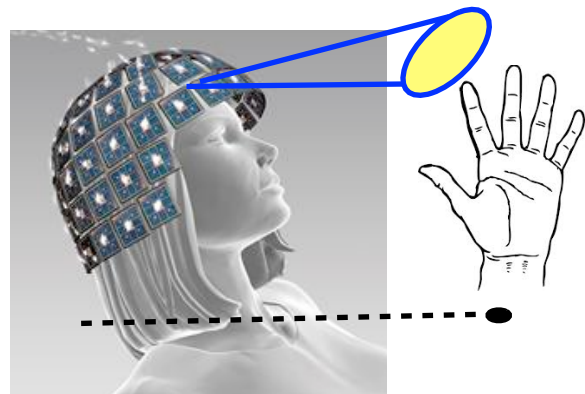
(Jones et al., *J Neurosci.* 2010; Sachett et al., *J. Neurosci.* 2015)



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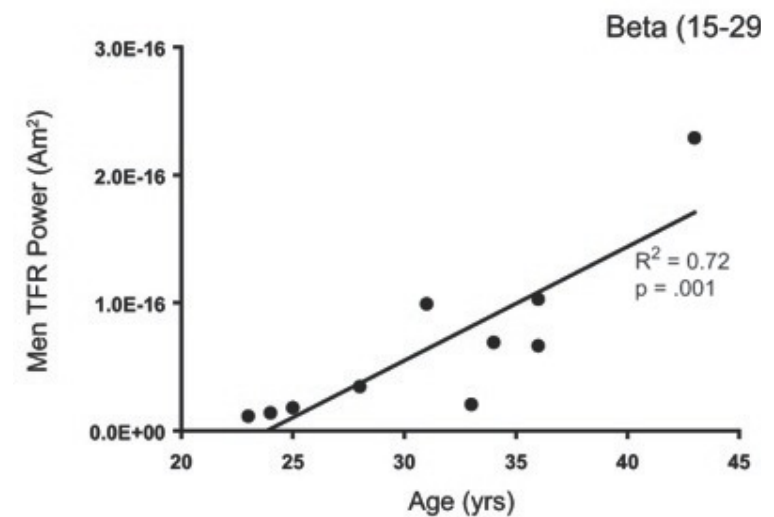
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- Beta increases with healthy adult aging.

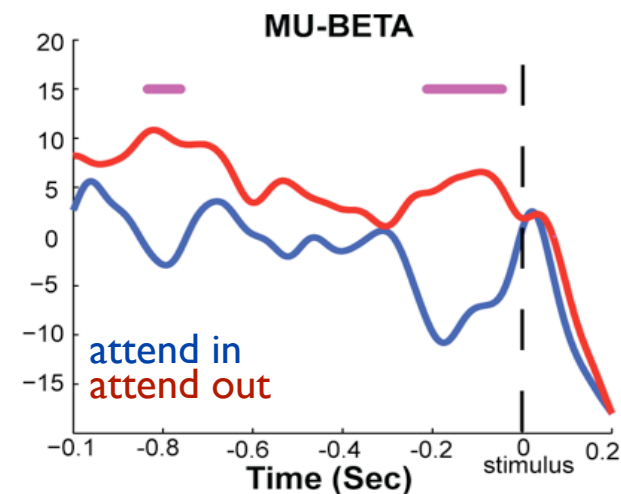
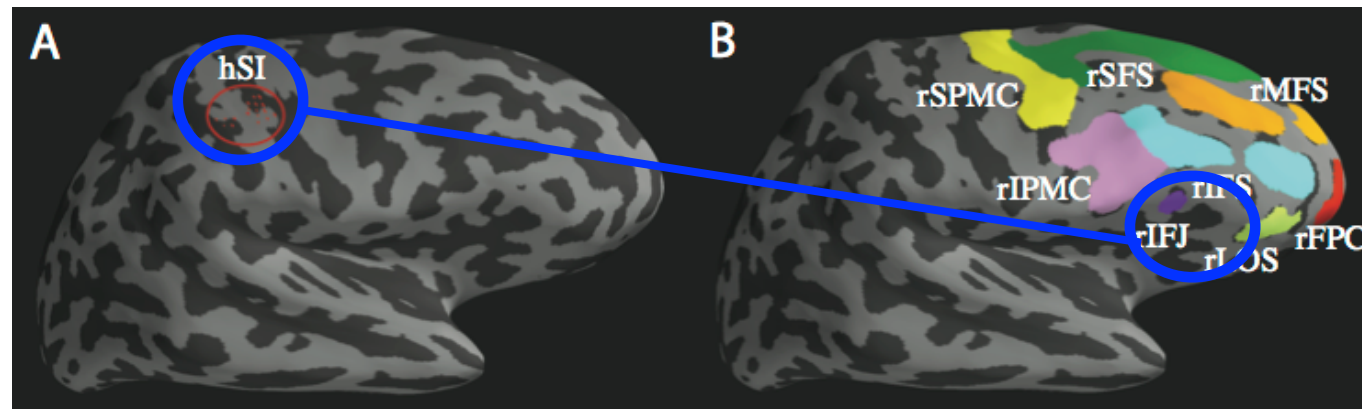
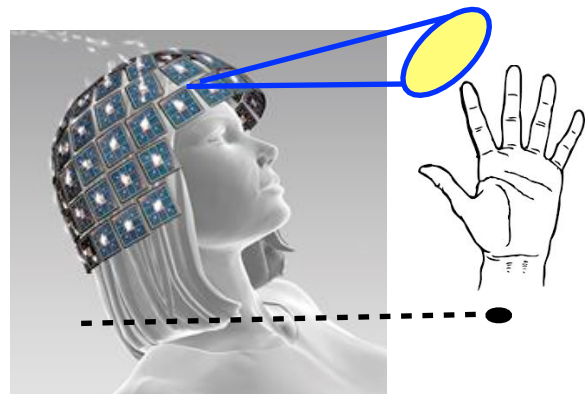
(Ziegler... Jones, *Neuroimage* 2010)



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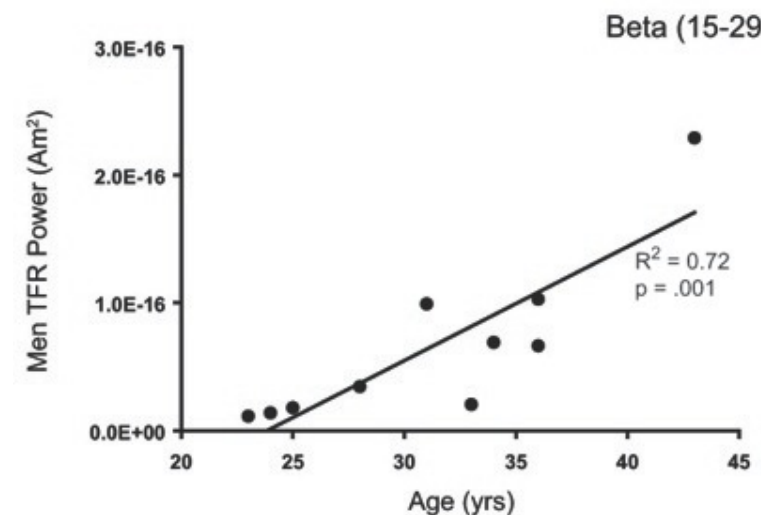
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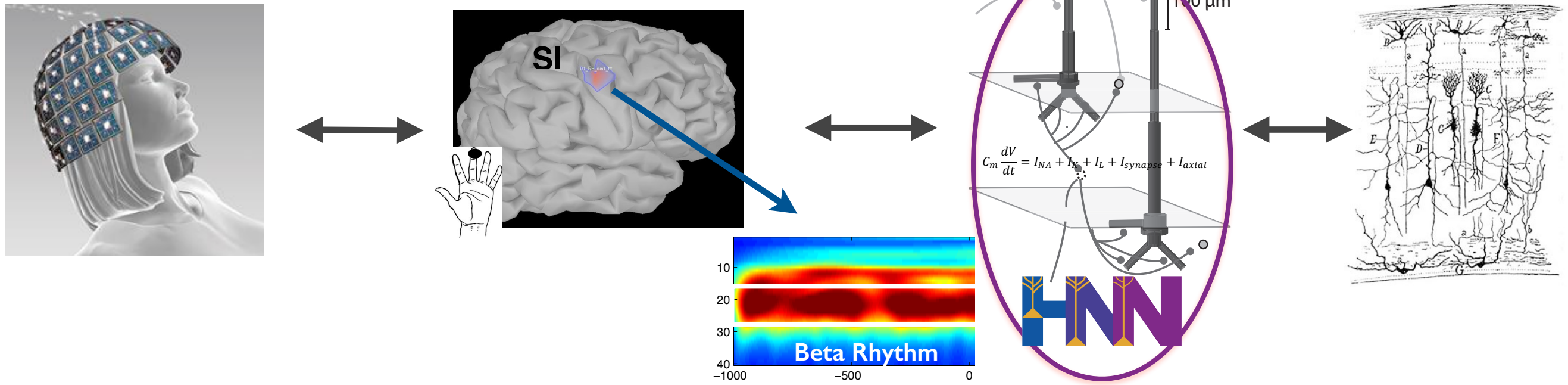


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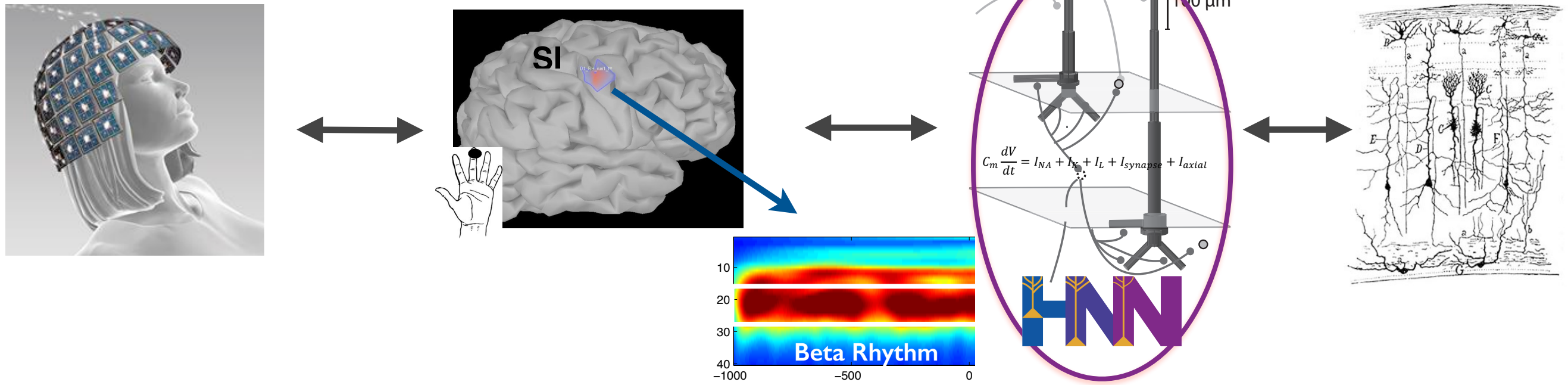
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Why does beta inhibit processing?

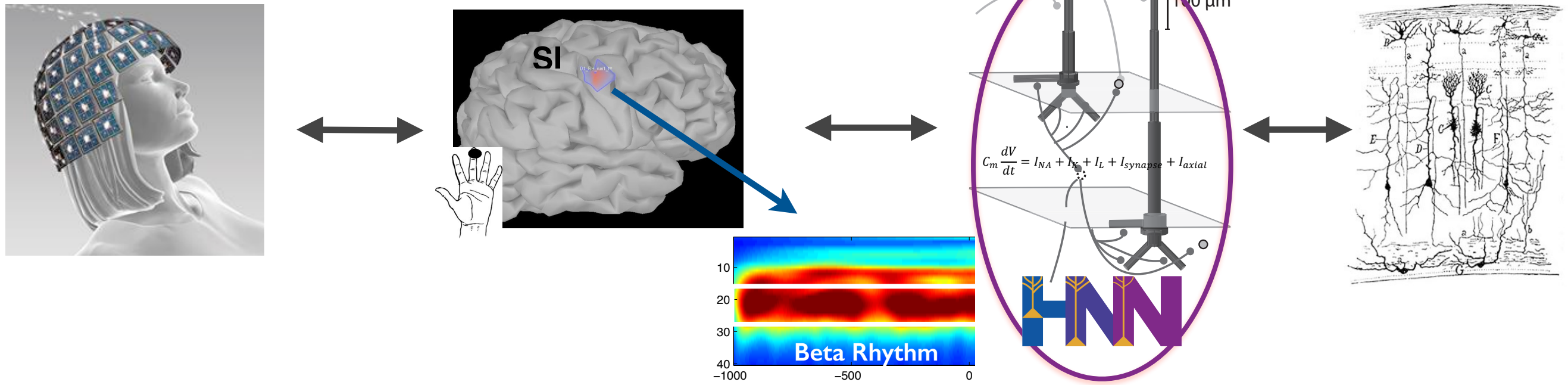


Applying HNN to study mechanisms by which beta inhibits perception



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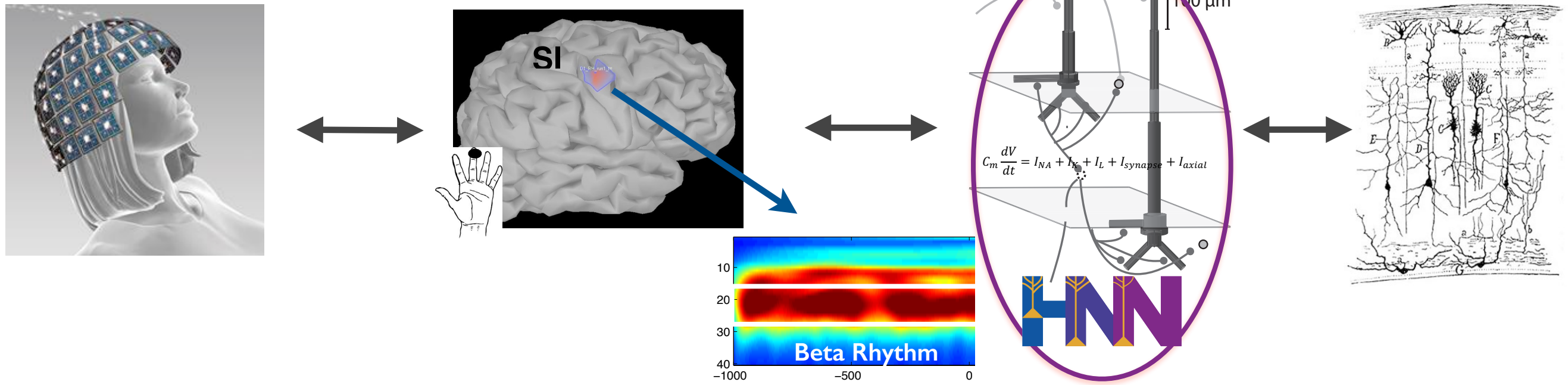
What does beta look like in *unaveraged* data?



Applying HNN to study mechanisms by which beta inhibits perception

What does beta look like in *unaveraged* data?

What features contribute to functionally relevant differences in average power?

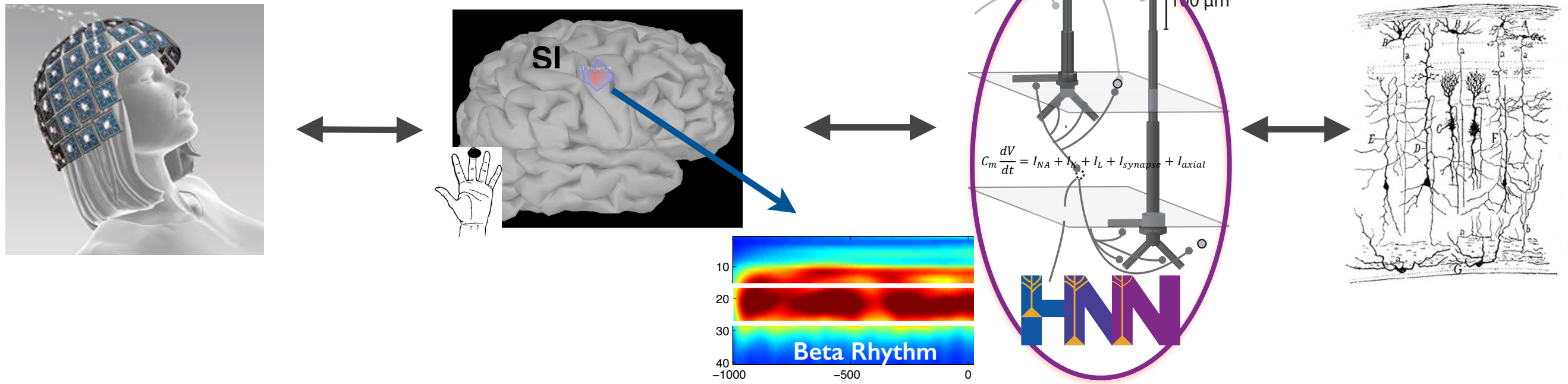


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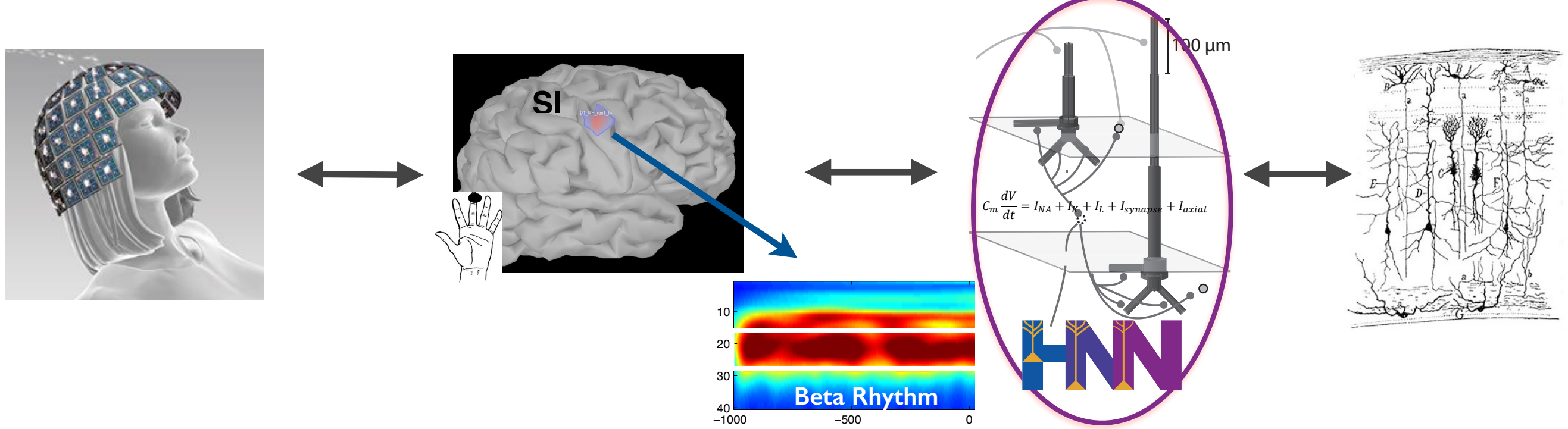
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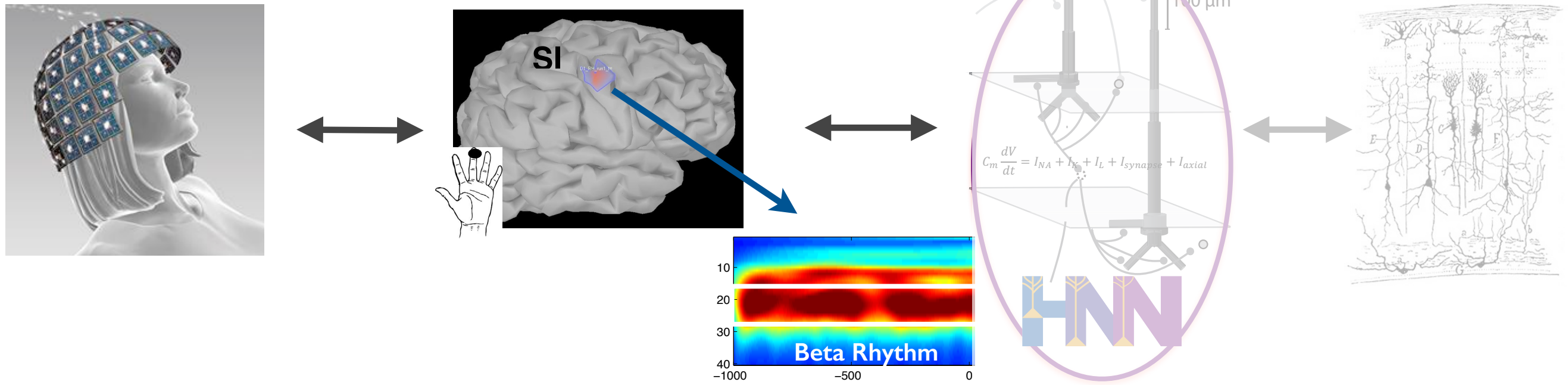
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New theory on the circuit level dynamics creating beta predicts beta decreases the salience of sensory input via layer specific recruitment of inhibition that decreases the relay of information.

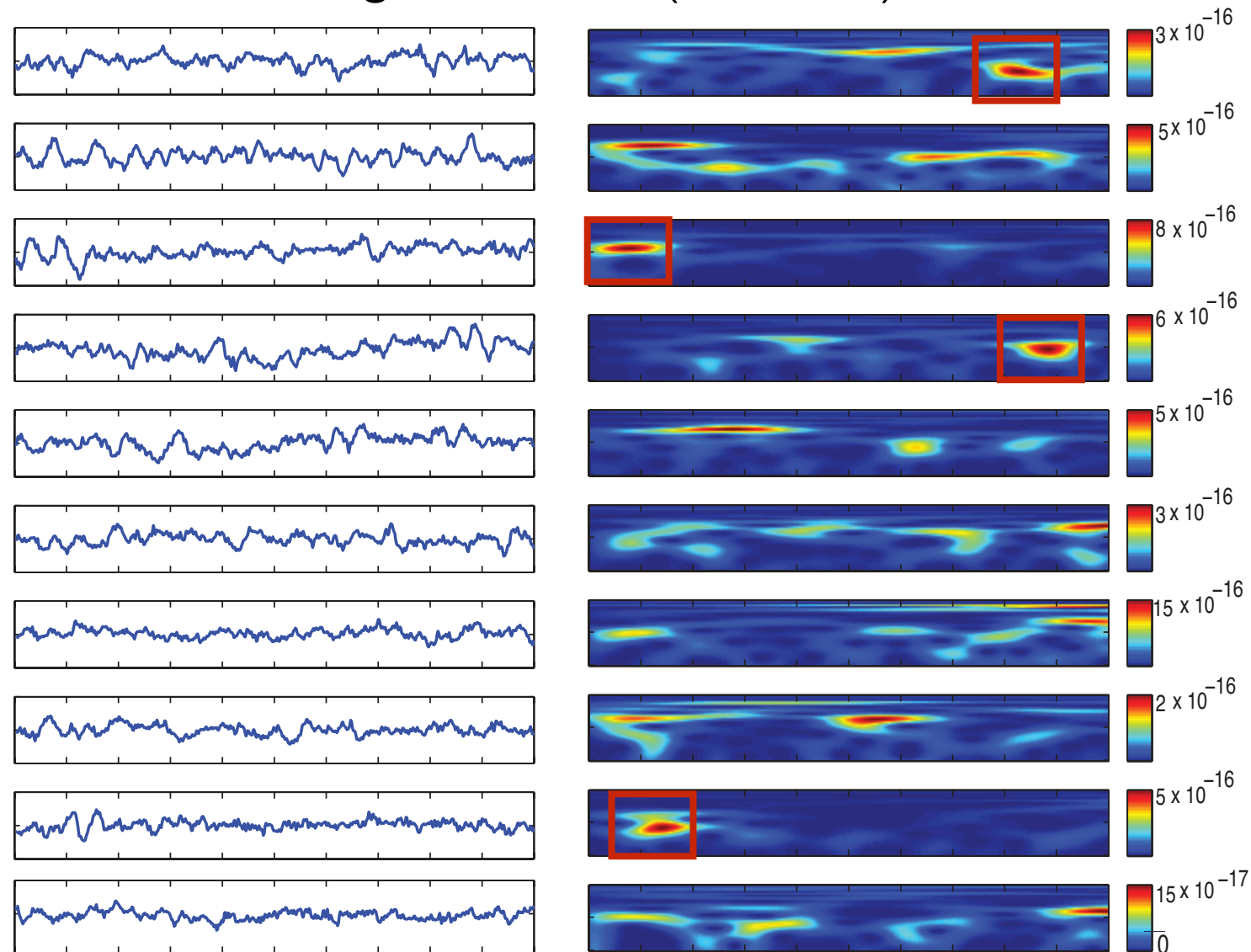


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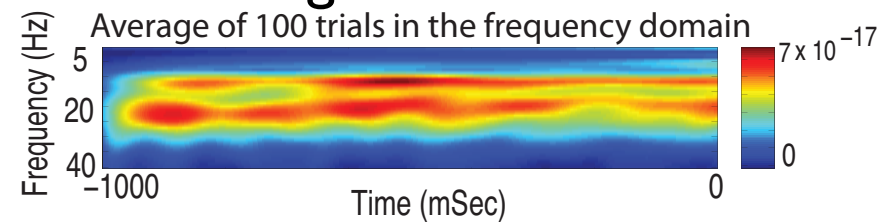
What does beta look like in unaveraged data?

Spontaneous Beta Rhythms Are Transient

Single Trial Data (1 Second)



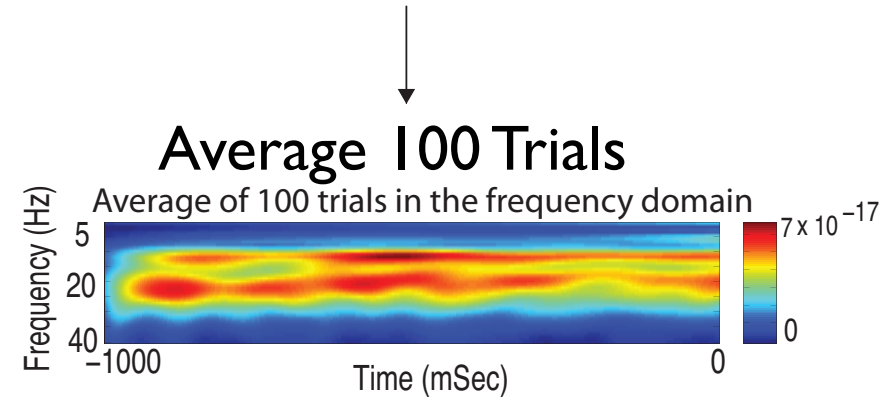
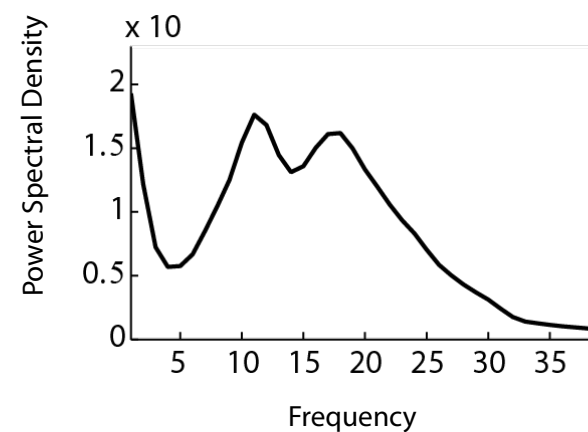
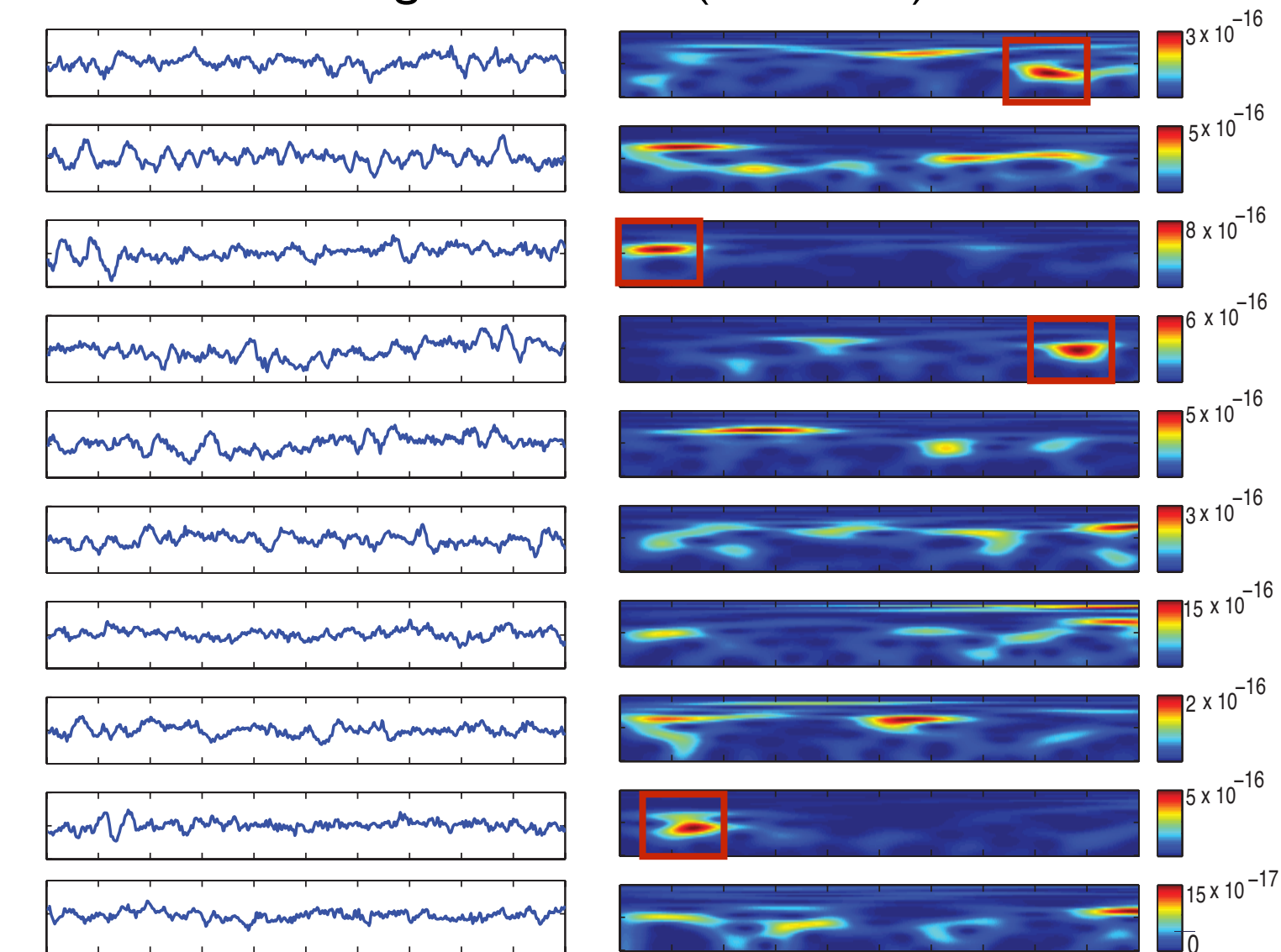
Average 100 Trials



Beta component of SI rhythm emerges as brief “events” ($<150\text{ms}$)

Spontaneous Beta Rhythms Are Transient

Single Trial Data (1 Second)



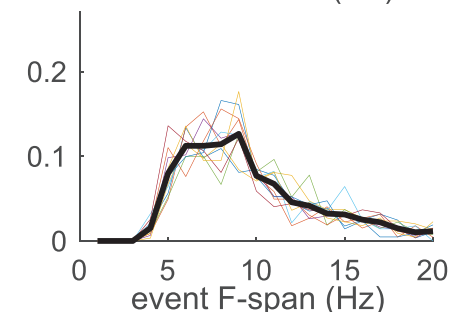
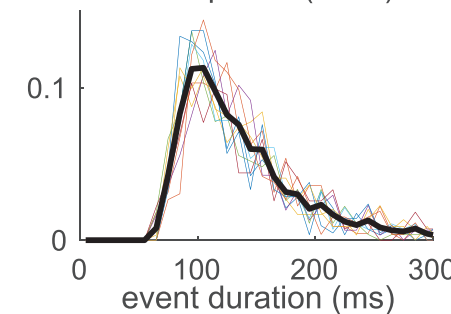
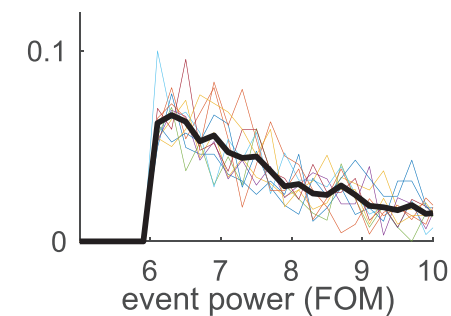
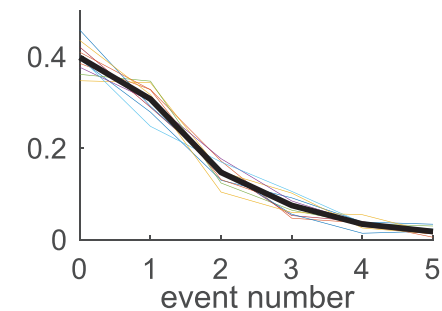
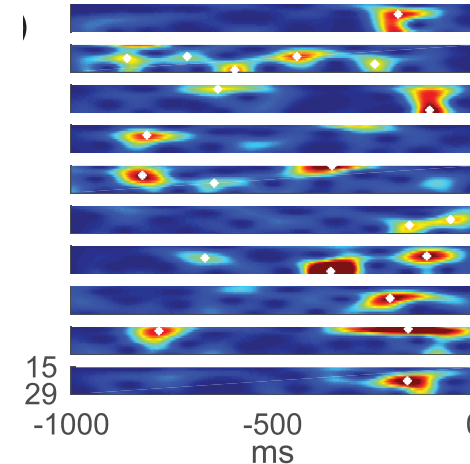
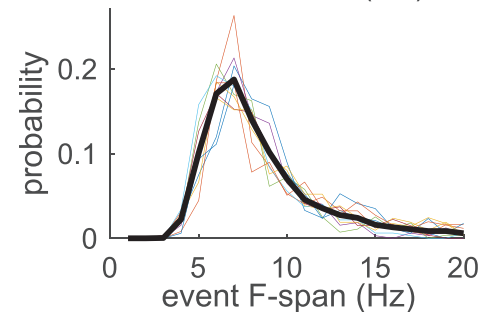
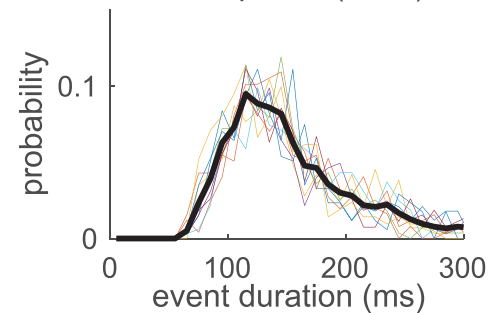
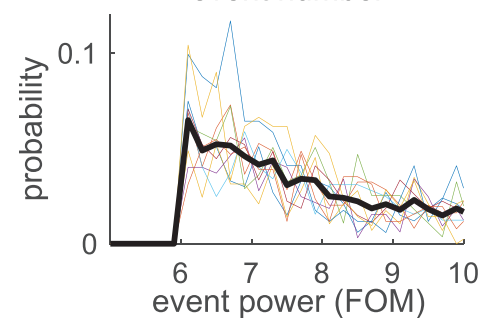
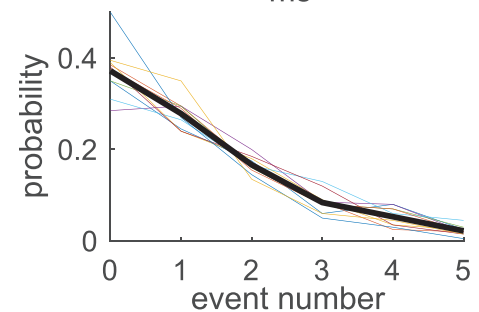
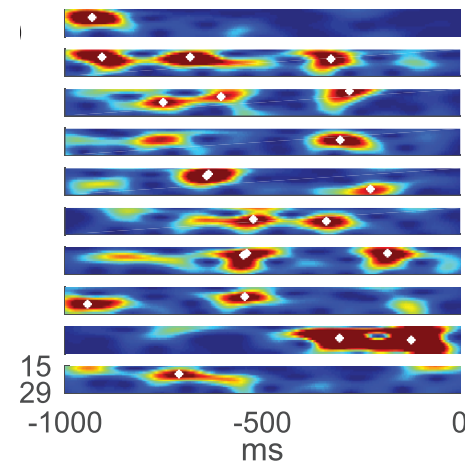
Beta component of SI rhythm emerges as brief “events” (<150ms)

Features of Transient Beta Events are Conserved Across Recording Modalities and Species

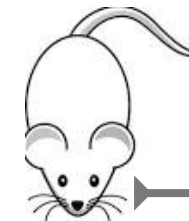
SI MEG



Human Detection Task



SI LFP



Mouse Detection Task

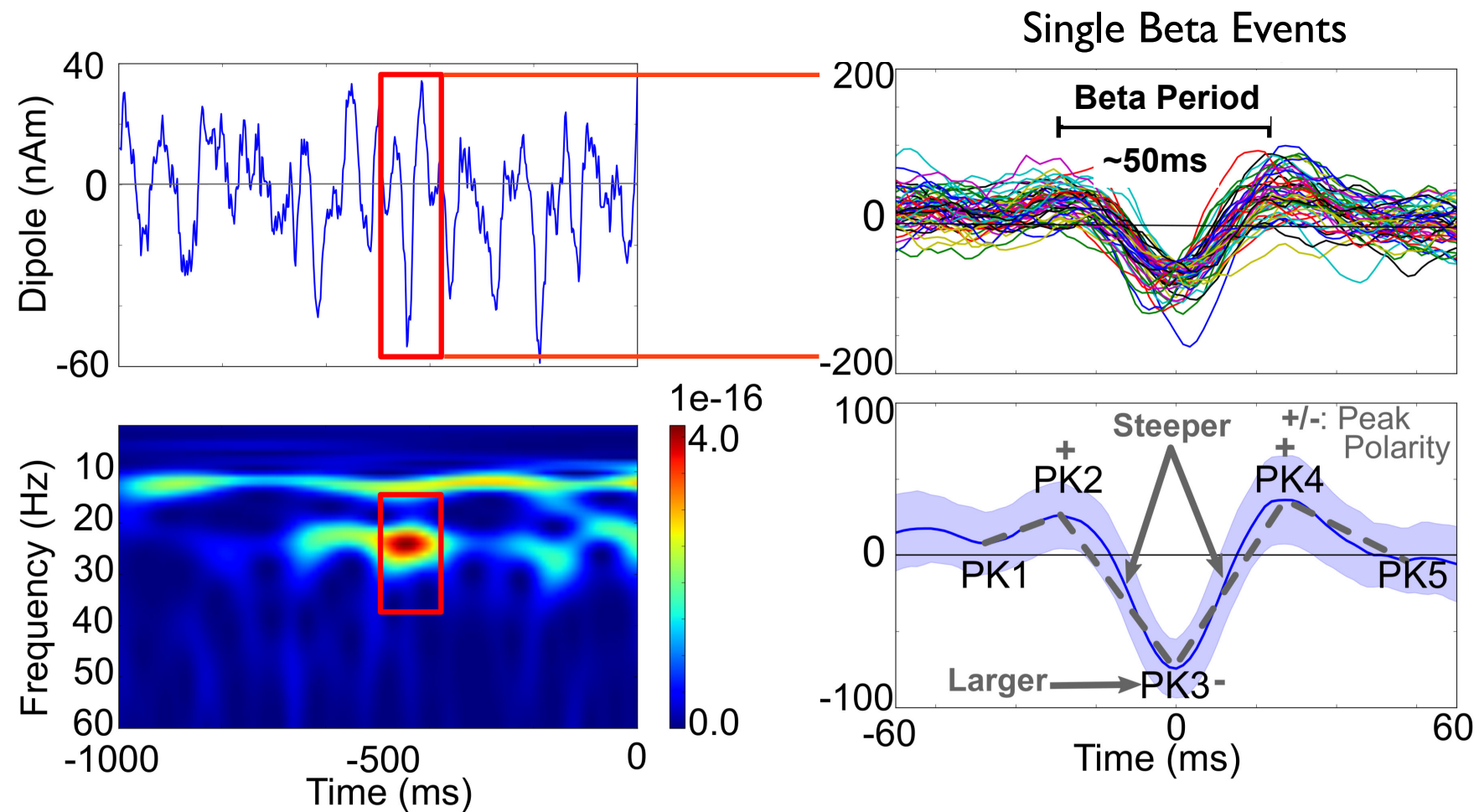
Chris Moore Lab Brown Univ.

Hyeyoung Shin

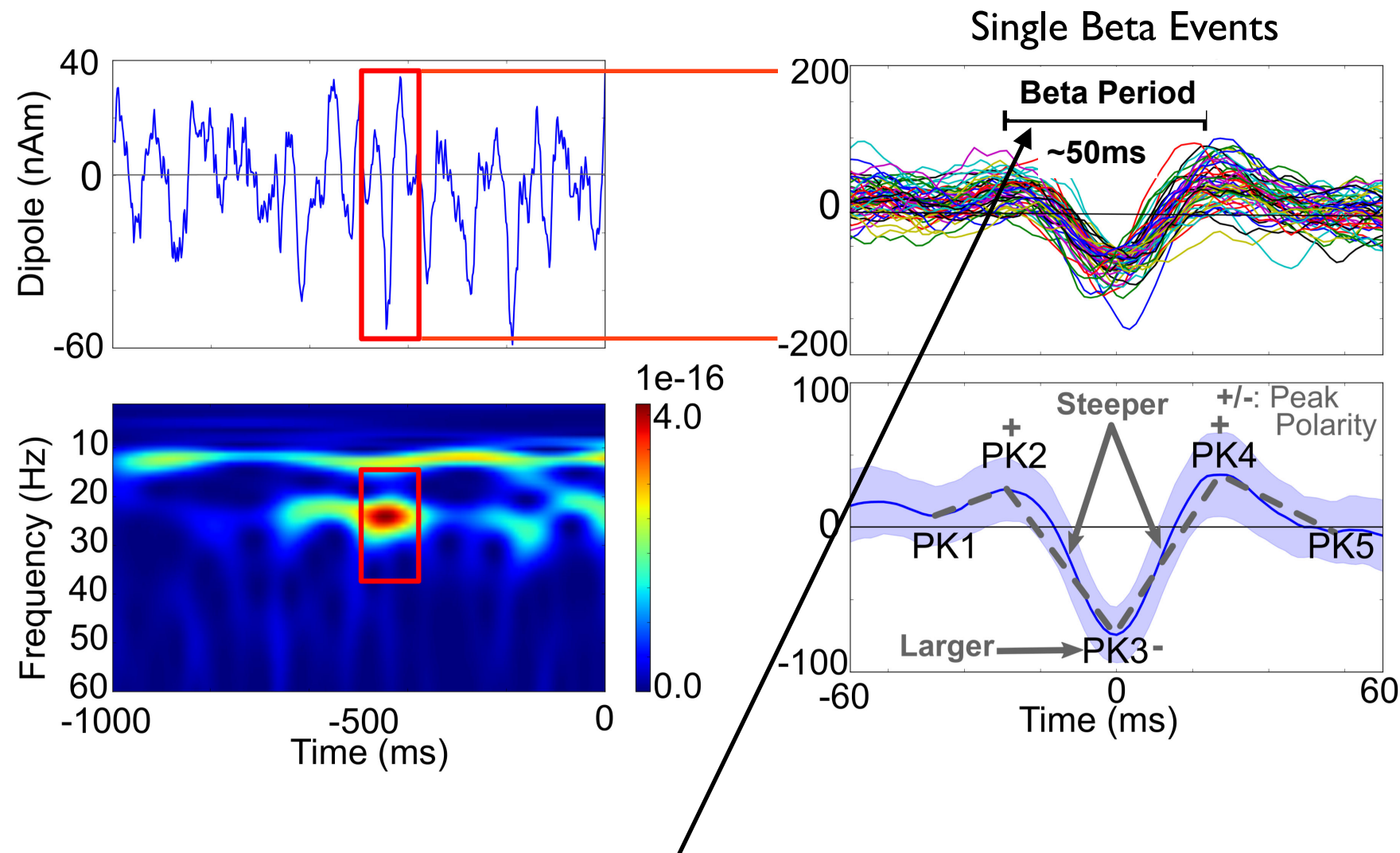
Shin... Jones *eLife* 2017

<https://github.com/jonescompneurolab/SpectralEvents>

MEG Beta “Events” Have Stereotypical Waveforms

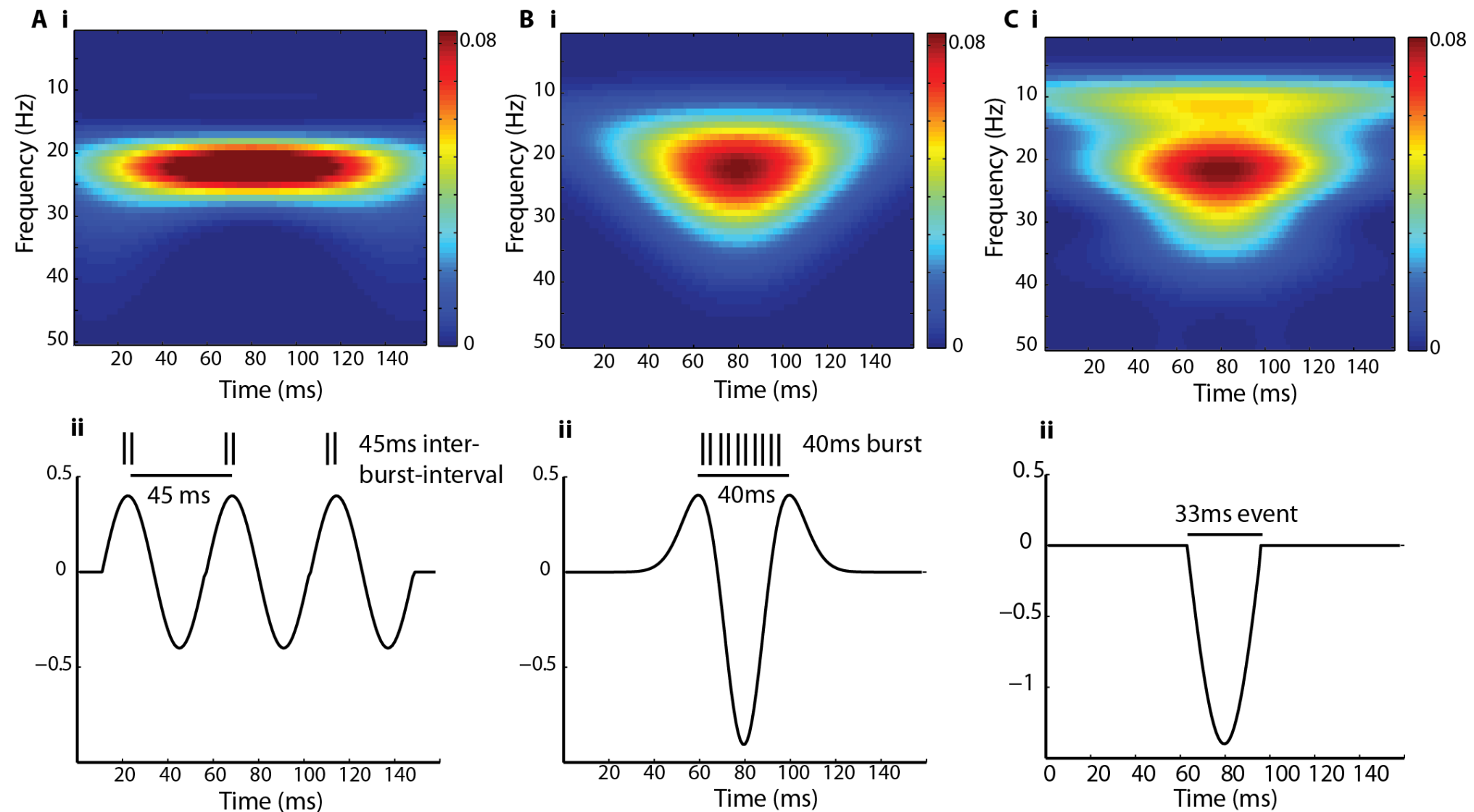


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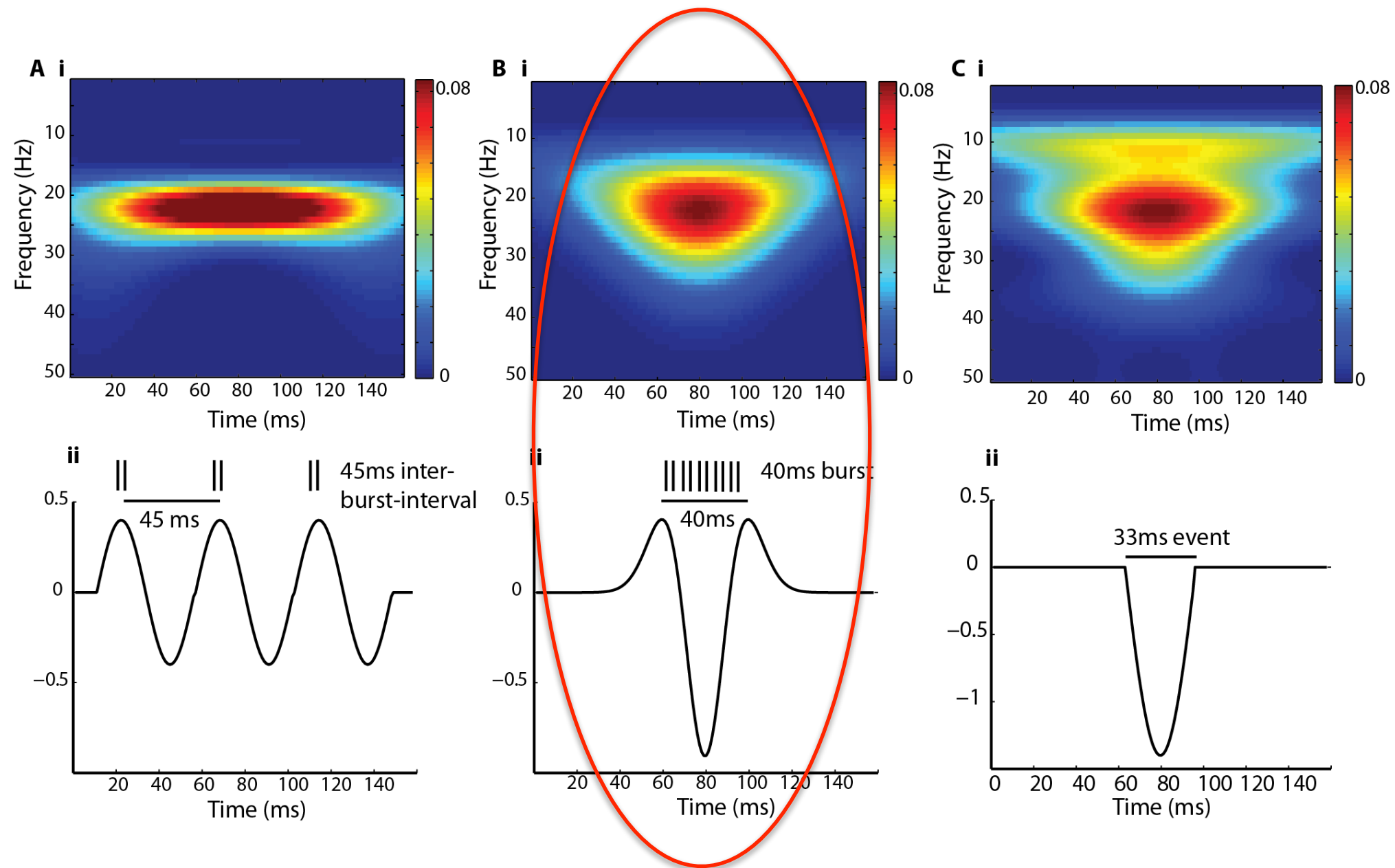


Beta frequency determined by duration of dominant deflection that lasts one beta period ~50ms.

Different Waveform Shapes Can Give Similar Frequency Response with Vastly Different Circuit Mechanisms

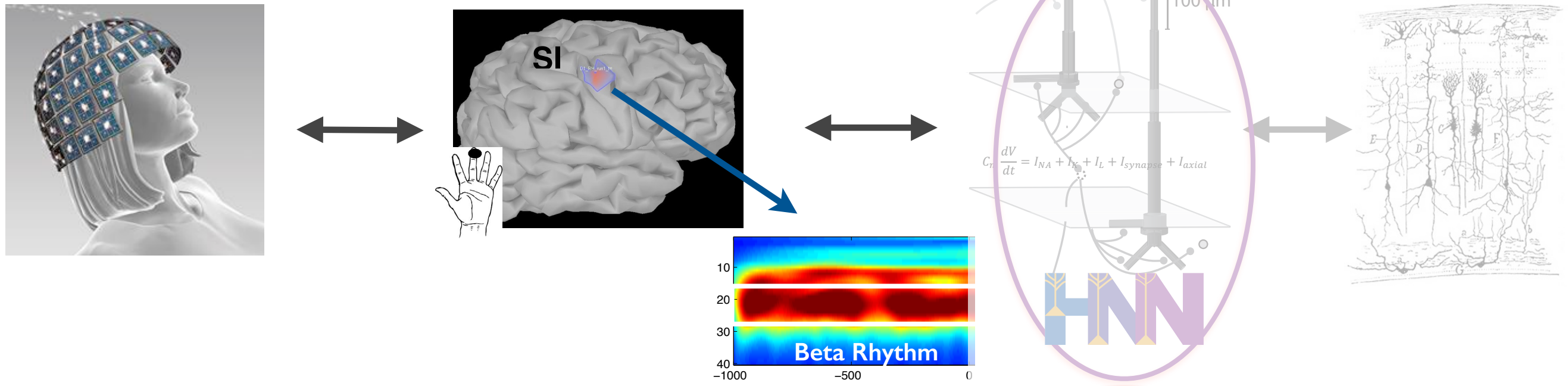


Different Waveform Shapes Can Give Similar Frequency Response with Vastly Different Circuit Mechanisms



MEG Beta Event Waveform (Sherman... Jones, *PNAS* 2016)

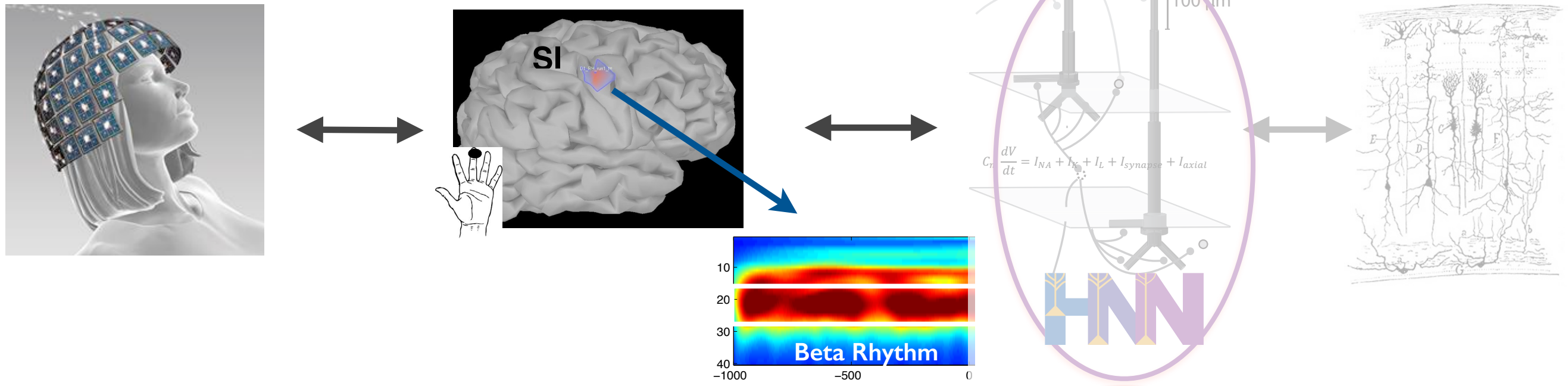
* Cole ... Voytex *J. Neurosci* 2017: MI beta events in Parkinson's Disease patients have "sharper" peaks; normalized by DBS



Applying HNN to study mechanisms by which beta inhibits perception

What does beta look like in *unaveraged* data?

Beta “events” are transient (<150ms) with a stereotypical waveform.



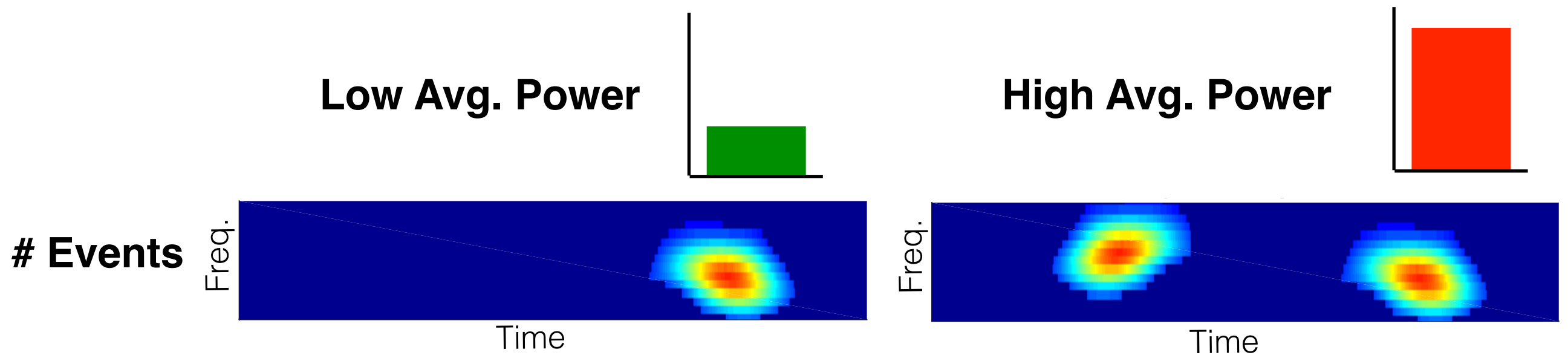
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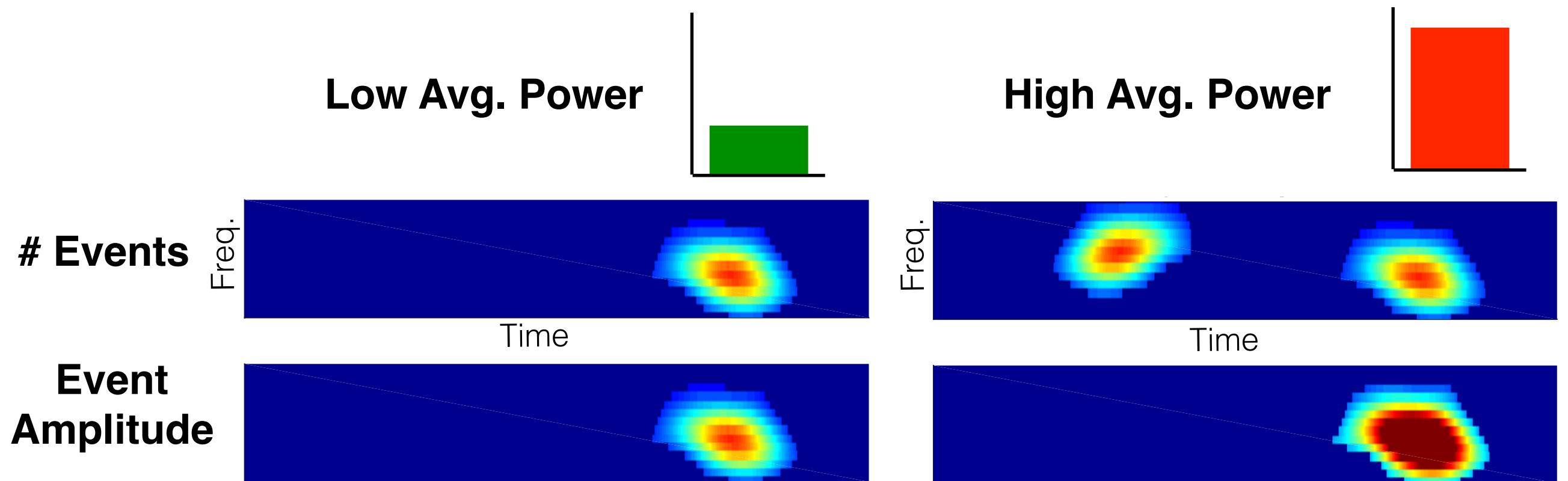
Beta “events” are transient (<150ms) with a stereotypical waveform.

What features underly functionally relevant differences in average power?

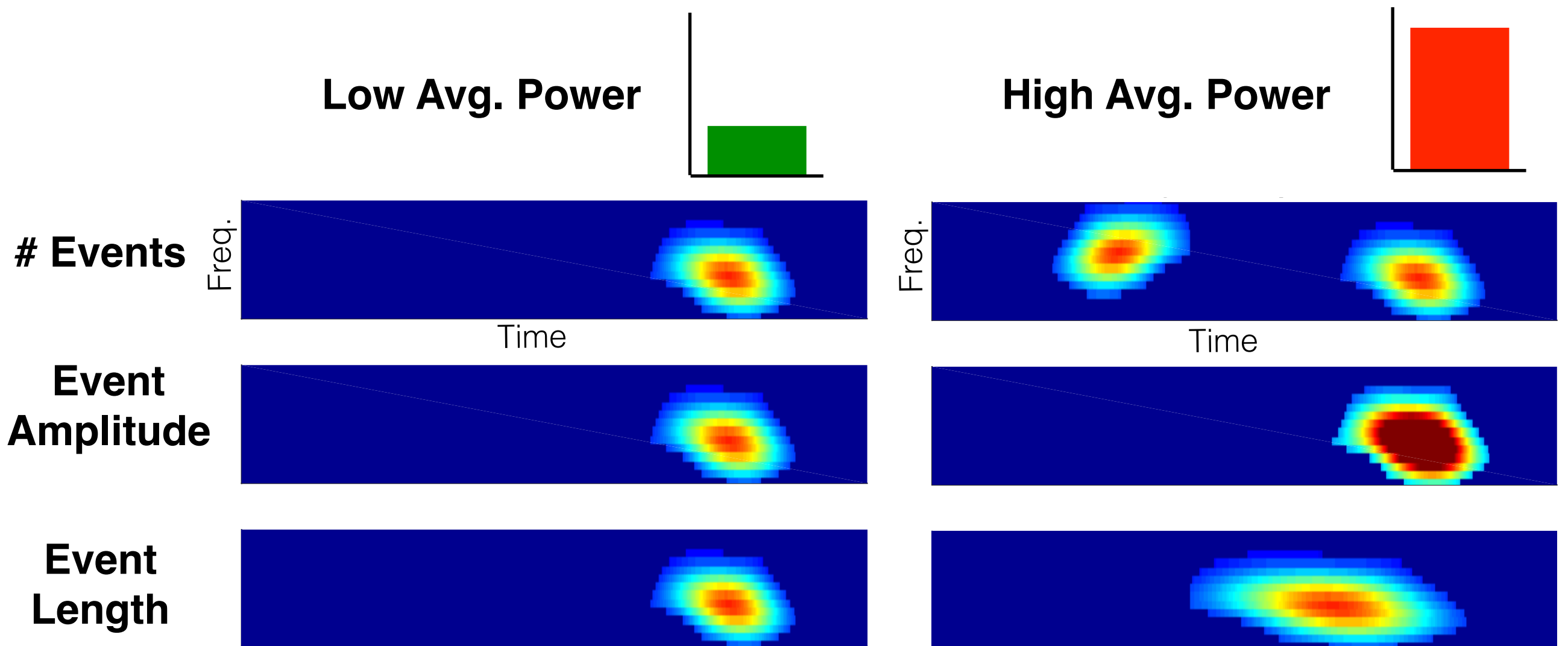
Possible Features Underlying Differences in Average Beta Power



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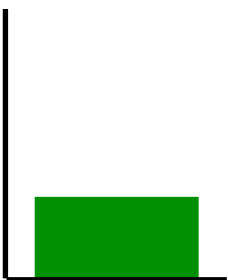


Possible Features Underlying Differences in Average Beta Power

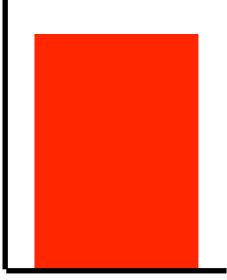


Possible Features Underlying Differences in Average Beta Power

Low Avg. Power

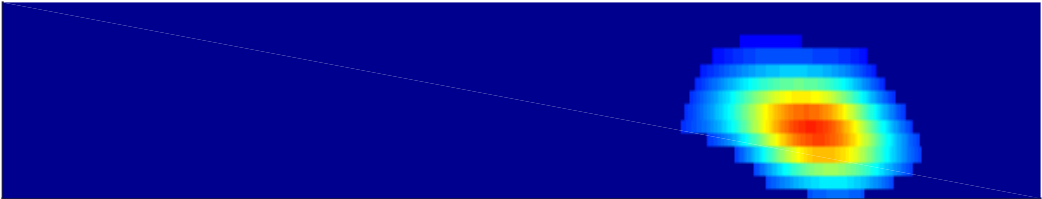


High Avg. Power



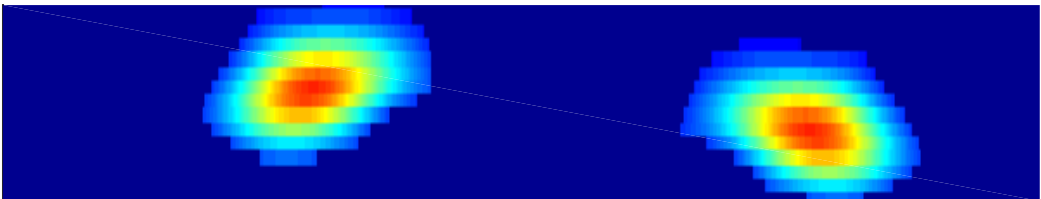
Events

Freq.



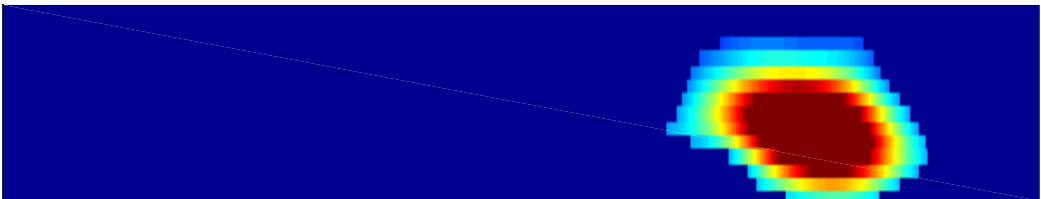
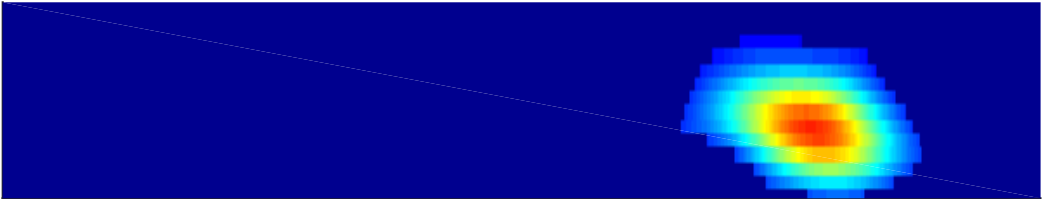
Time

Freq.

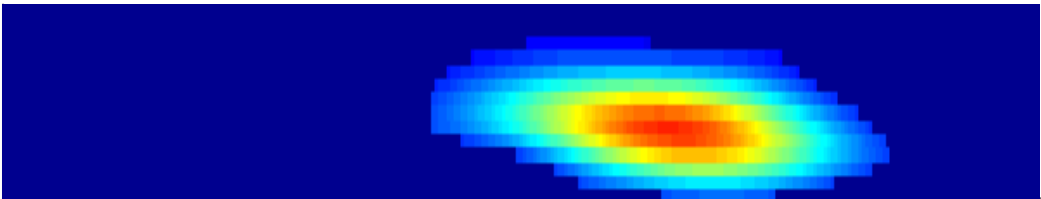


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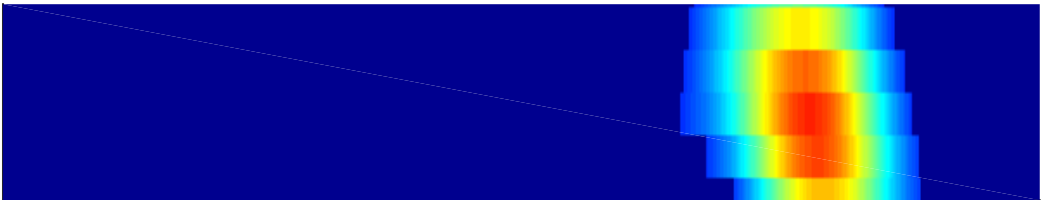
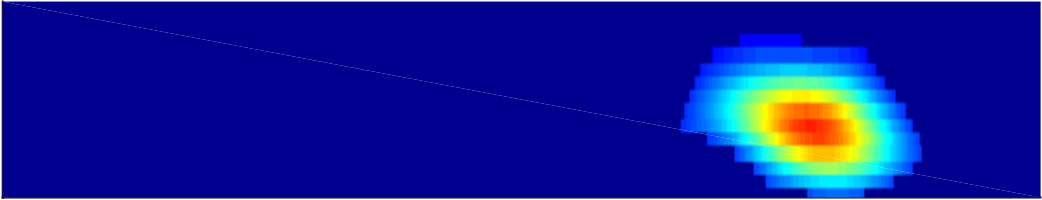
Event
Amplitude



Event
Length

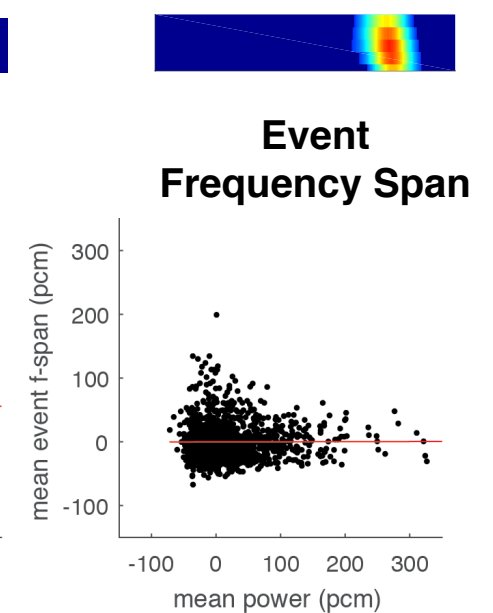
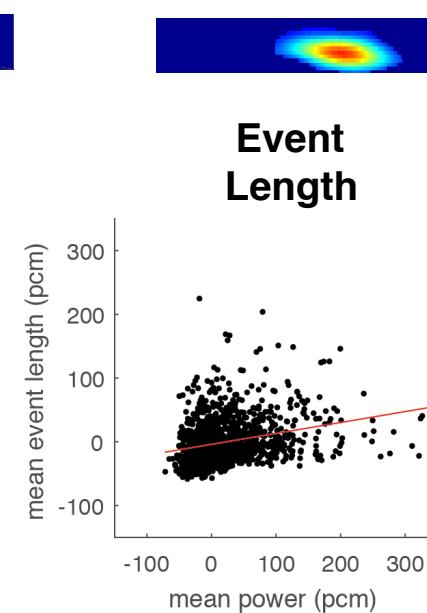
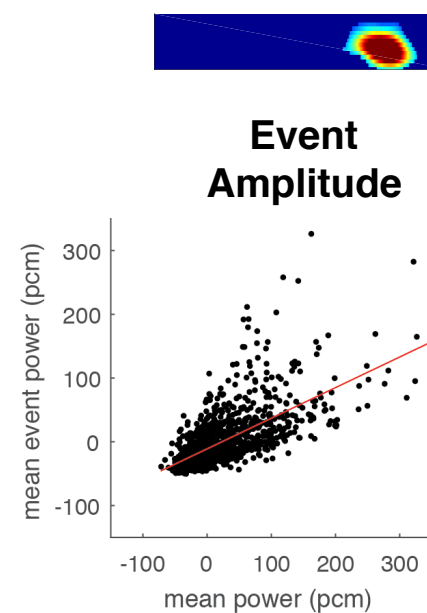
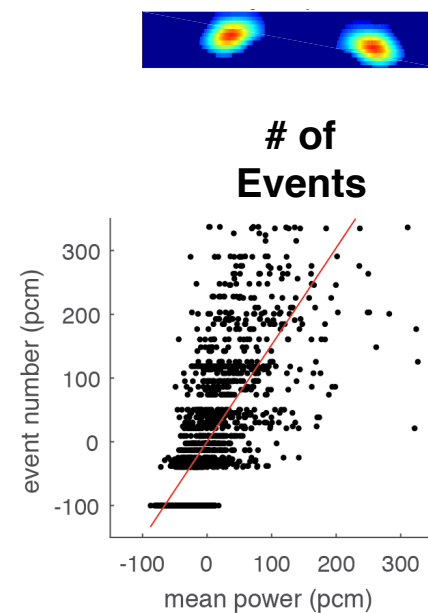
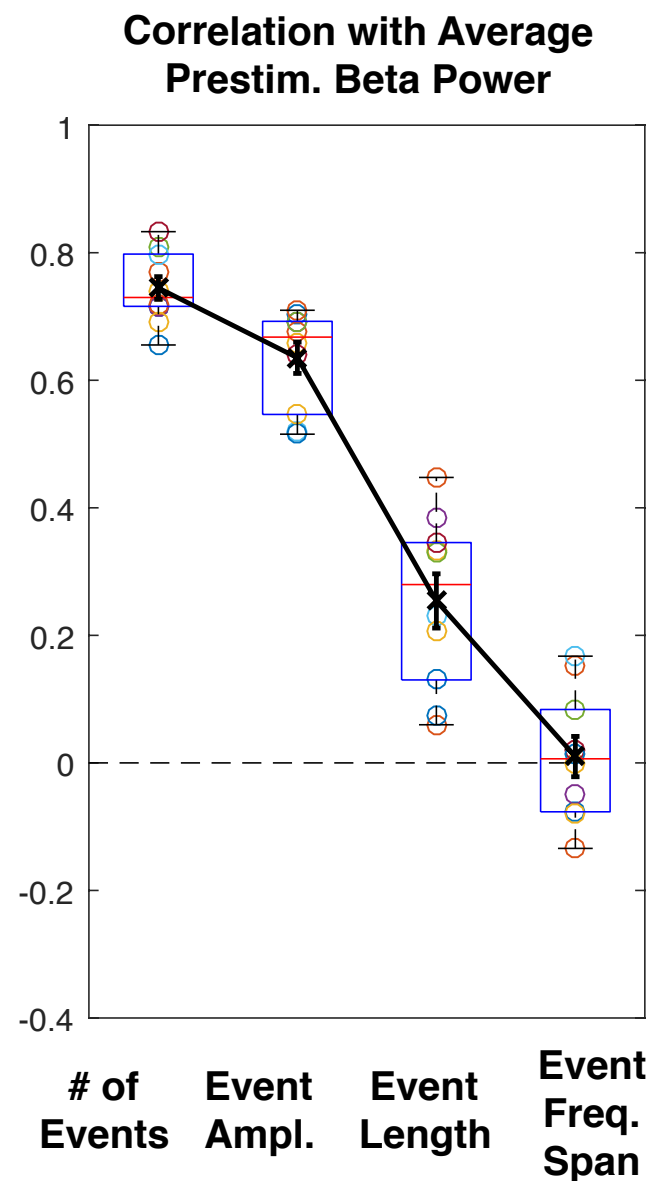


Event
Frequency
Span



Number of Beta Events Correlates Most with Avg. Power

Human SI MEG
Detection Task
Prestimulus Period

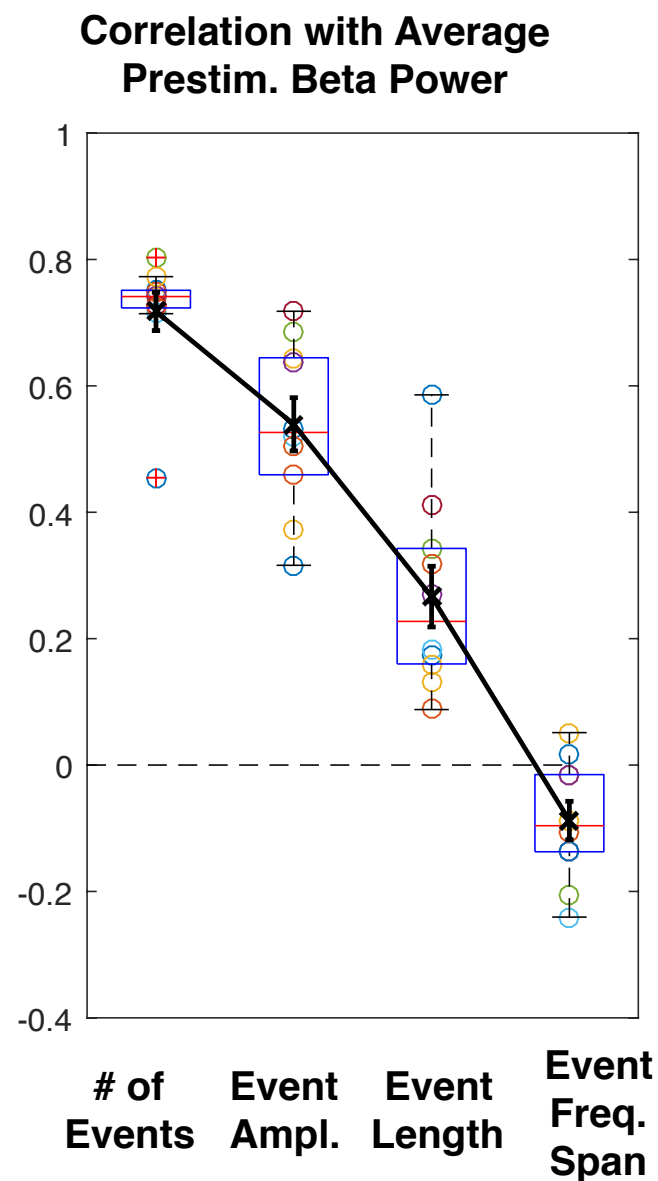
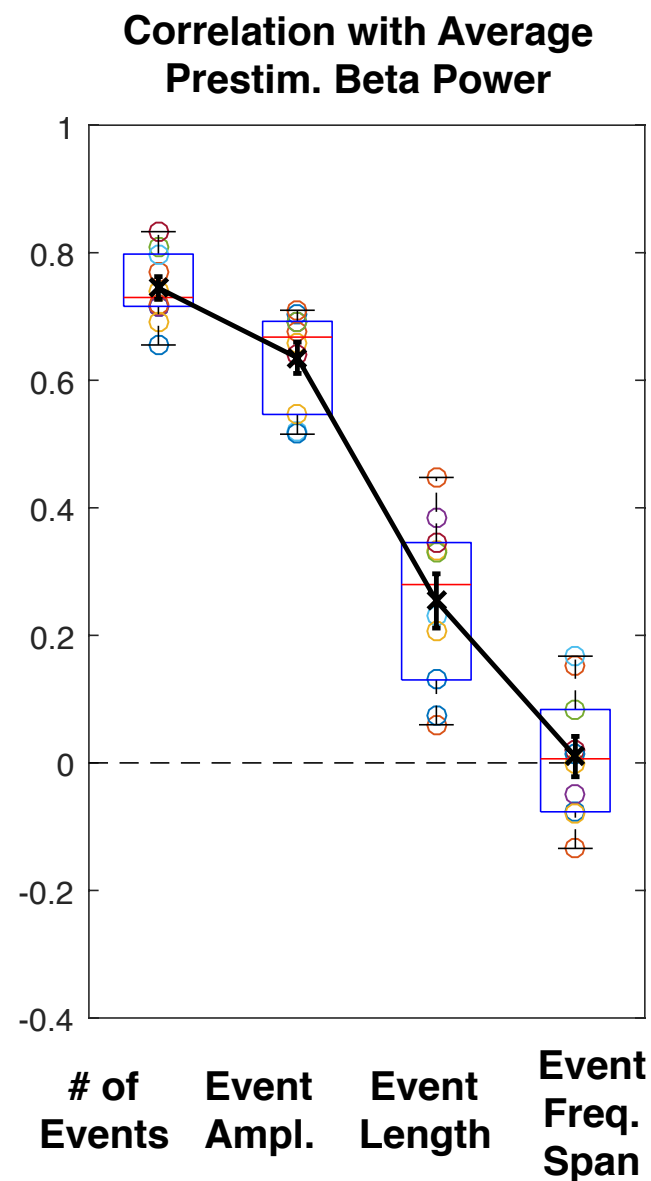
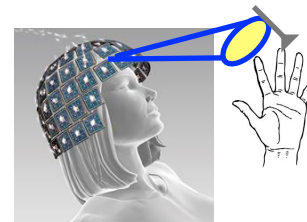


Number of Beta Events Correlates Most with Avg. Power

Human SI MEG
Detection Task
Prestimulus Period



Human SI MEG
Attention Task
Post-Cue/ Prestim. Period

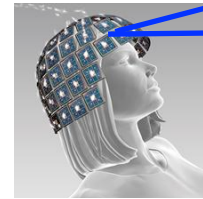


Number of Beta Events Correlates Most with Avg. Power

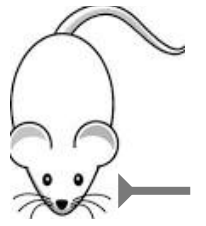
Human SI MEG
Detection Task
Prestimulus Period



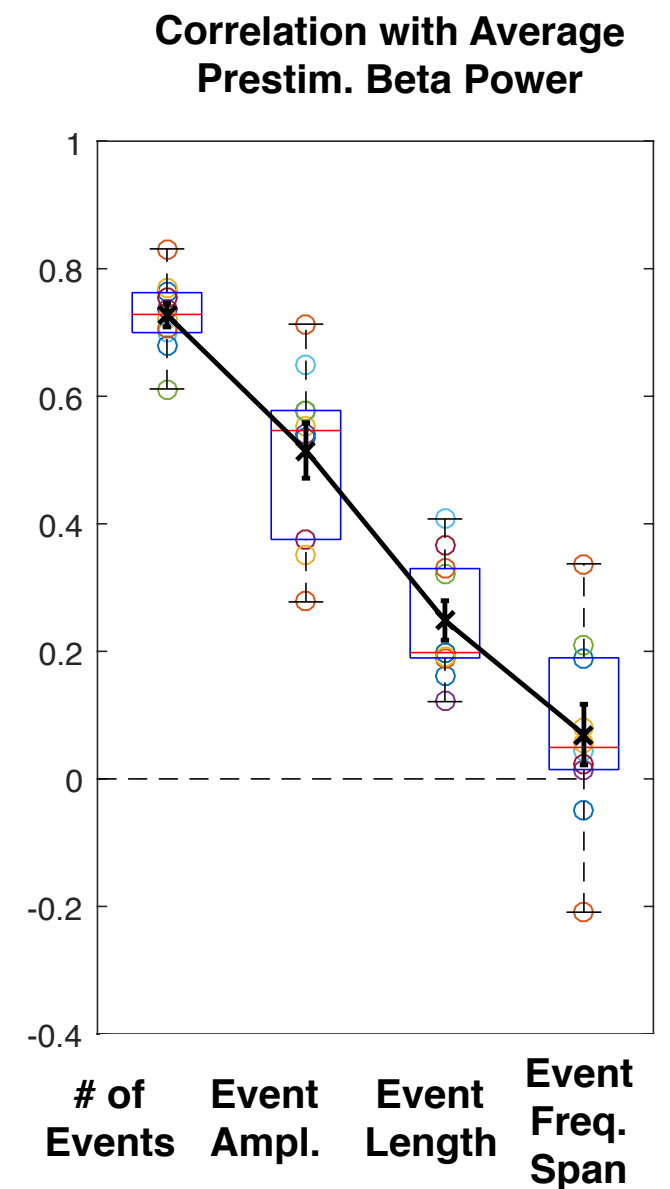
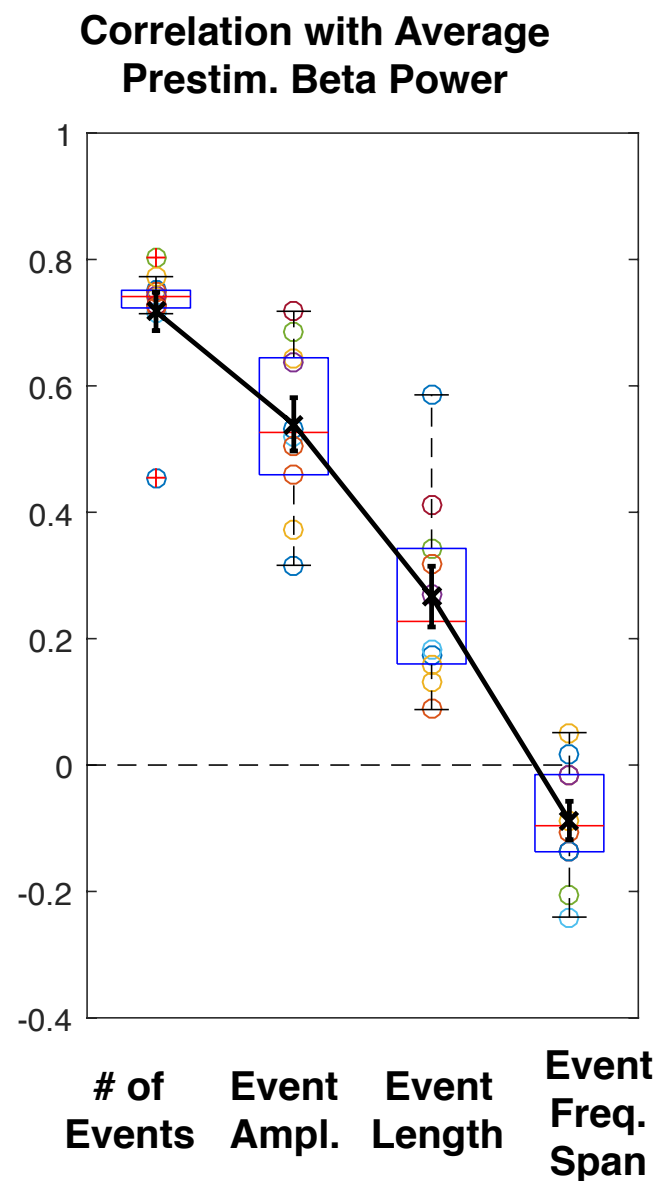
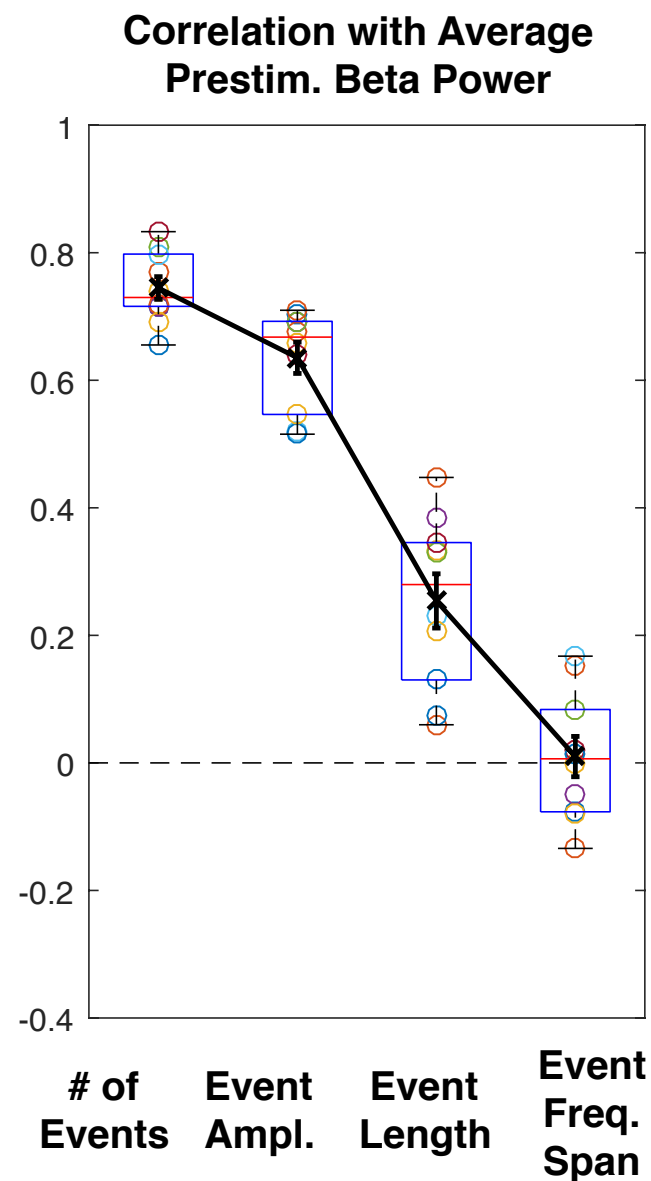
Human SI MEG
Attention Task
Post-Cue/ Prestim. Period



Mouse SI LFP
Detection Task
Prestimulus Period

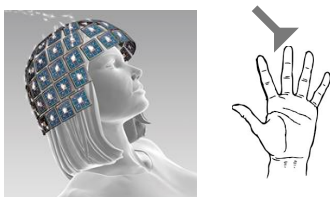


Moore Lab (Brown)

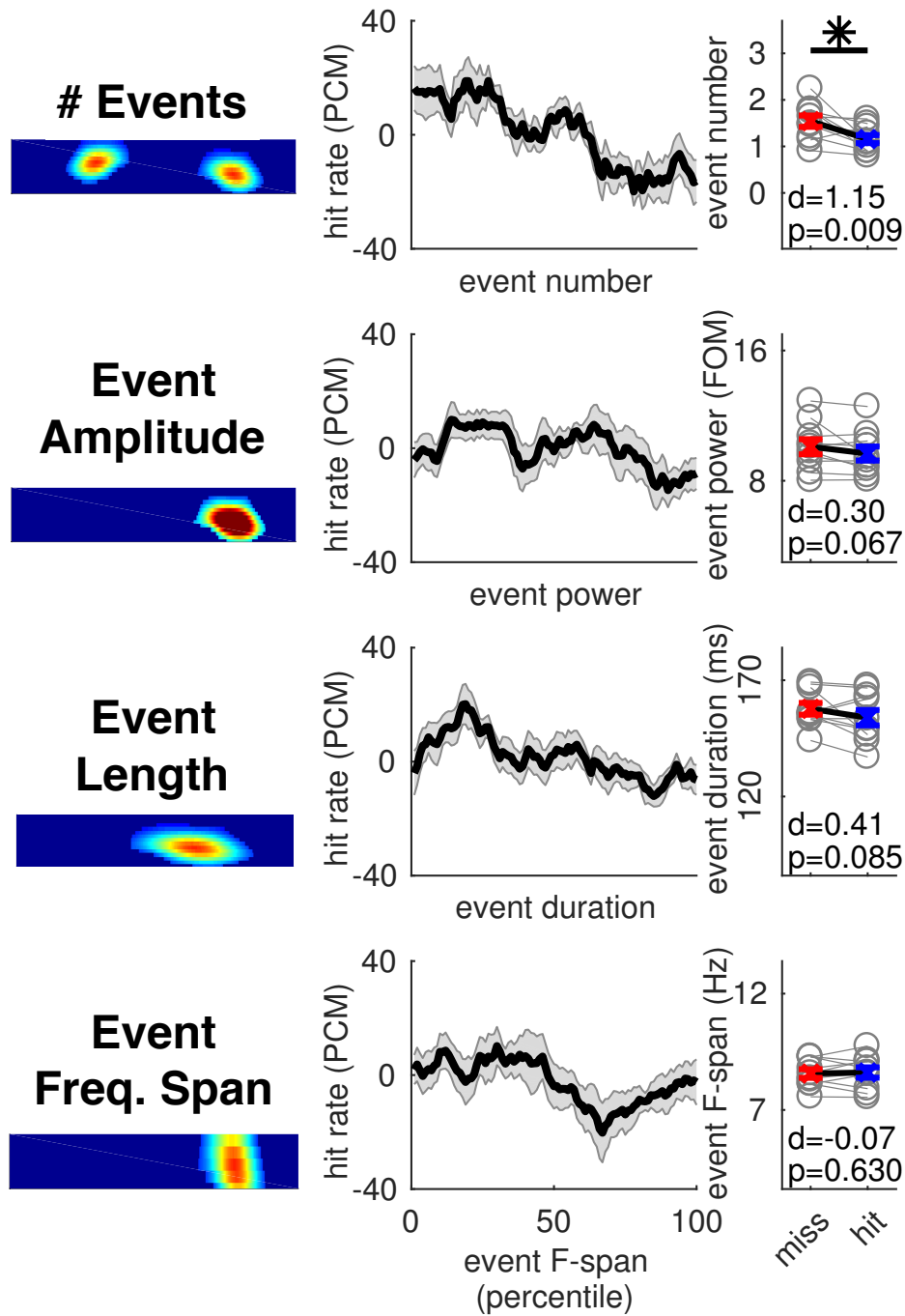


Trend is conserved across tasks and species

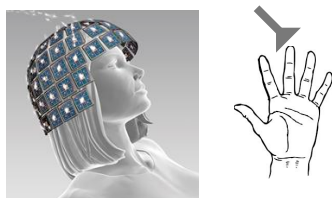
Number of Beta Events is Higher in Non-Detected / Non-Attended Trials



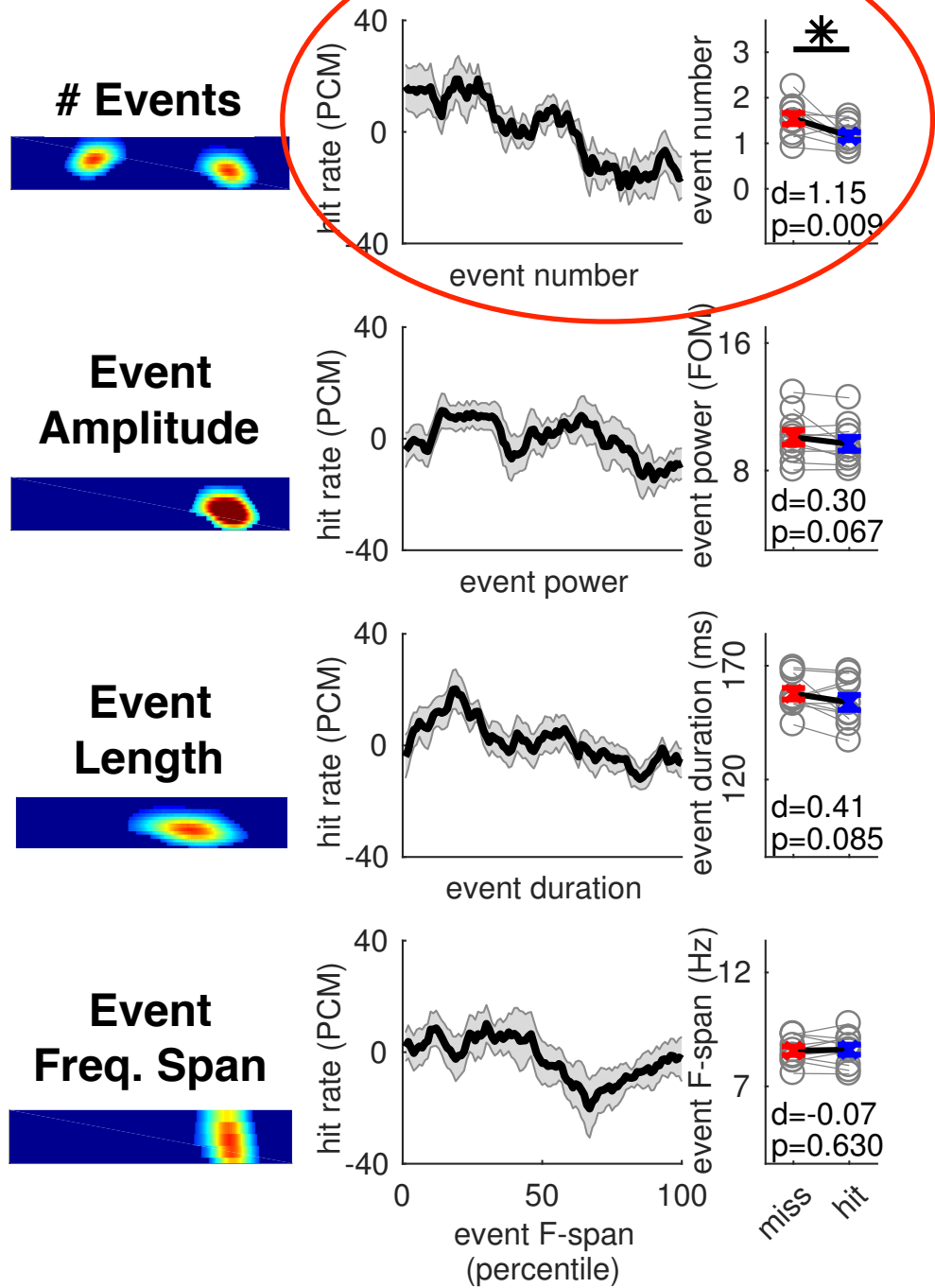
Human Detection Task



Number of Beta Events is Higher in Non-Detected / Non-Attended Trials



Human Detection Task

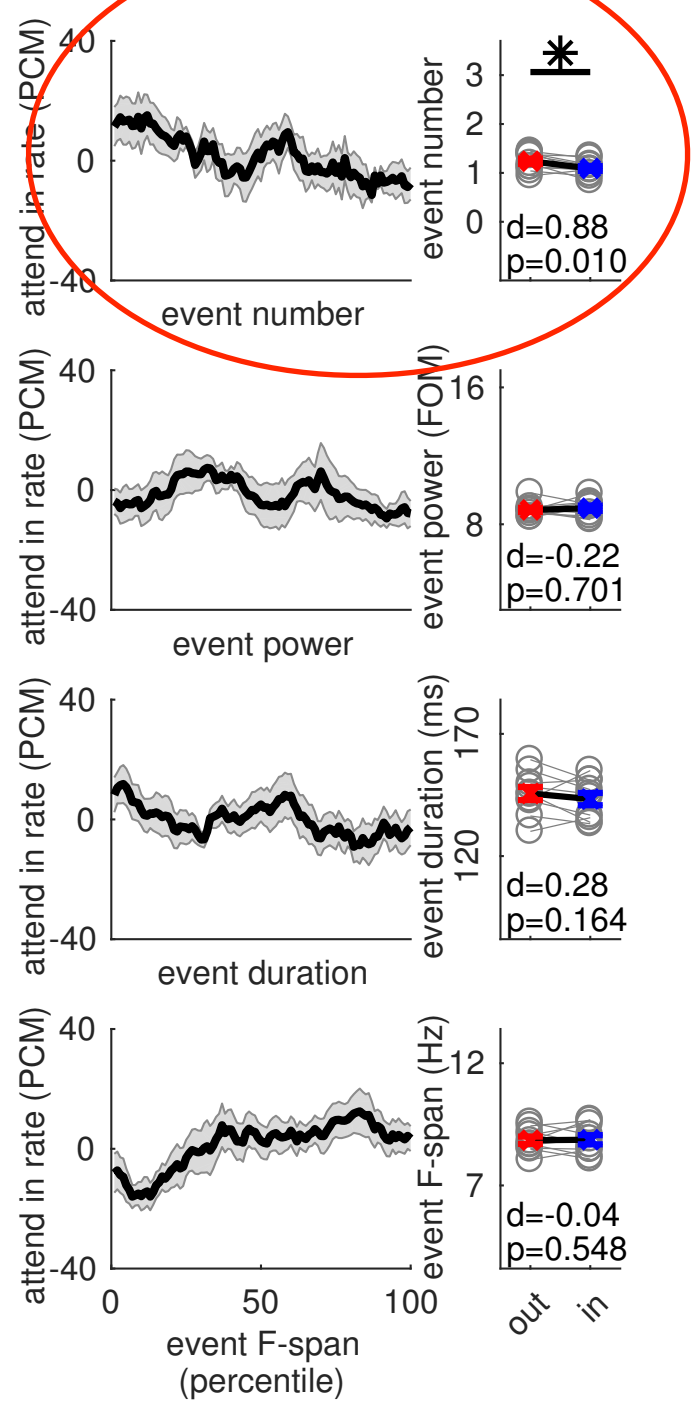
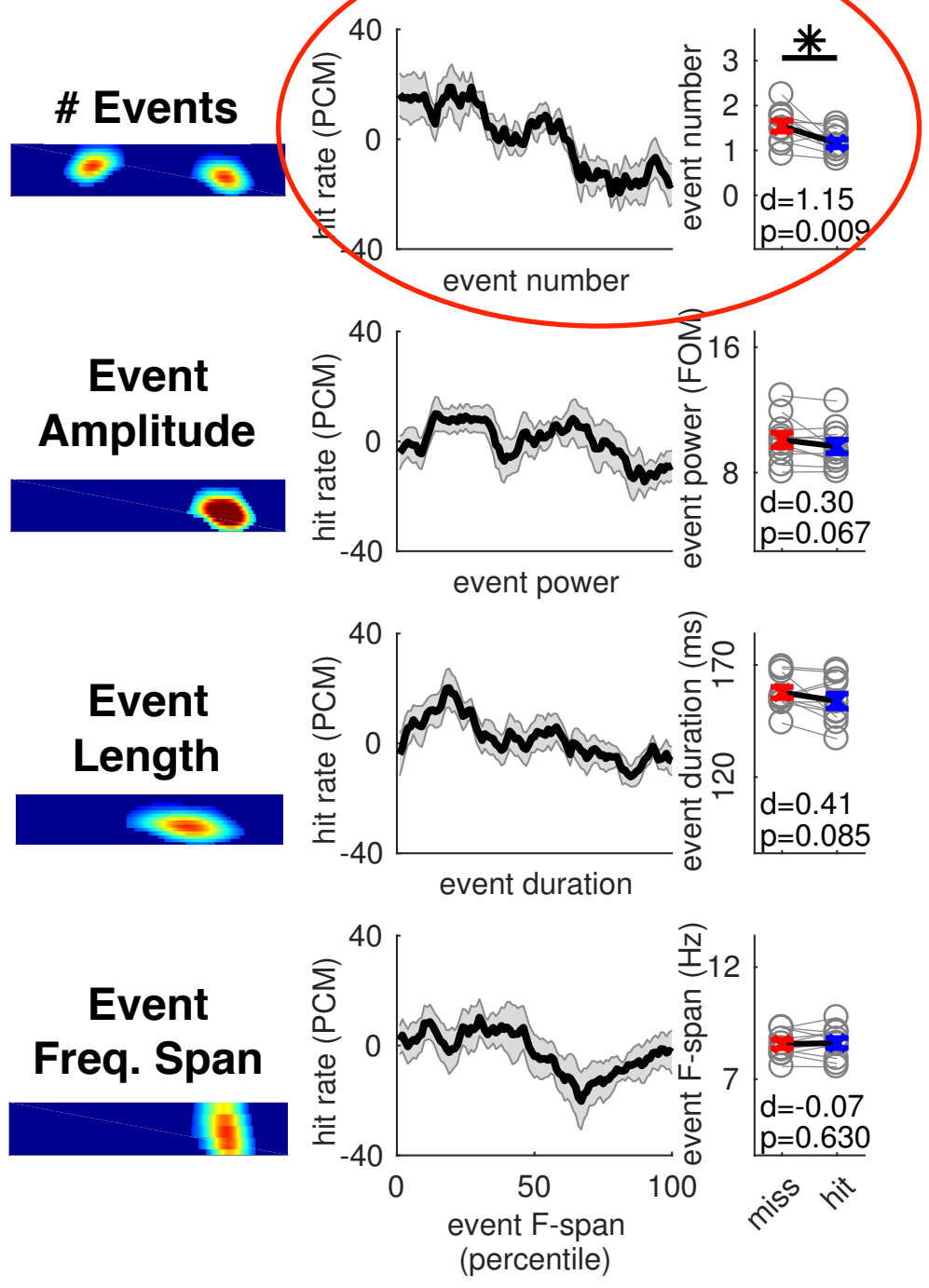


Number of Beta Events is Higher in Non-Detected / Non-Attended Trials

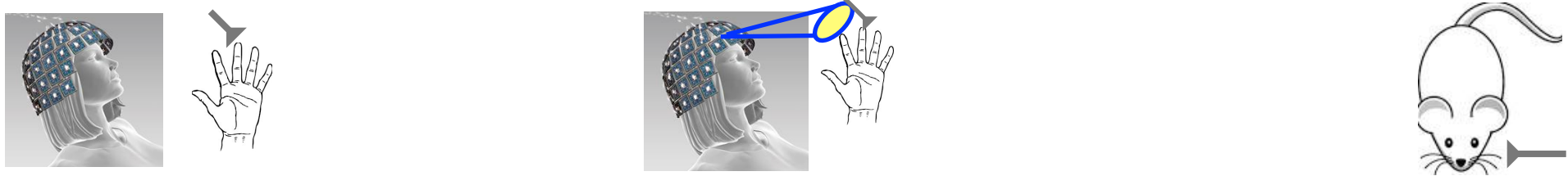


Human Detection Task

Human Attention Task



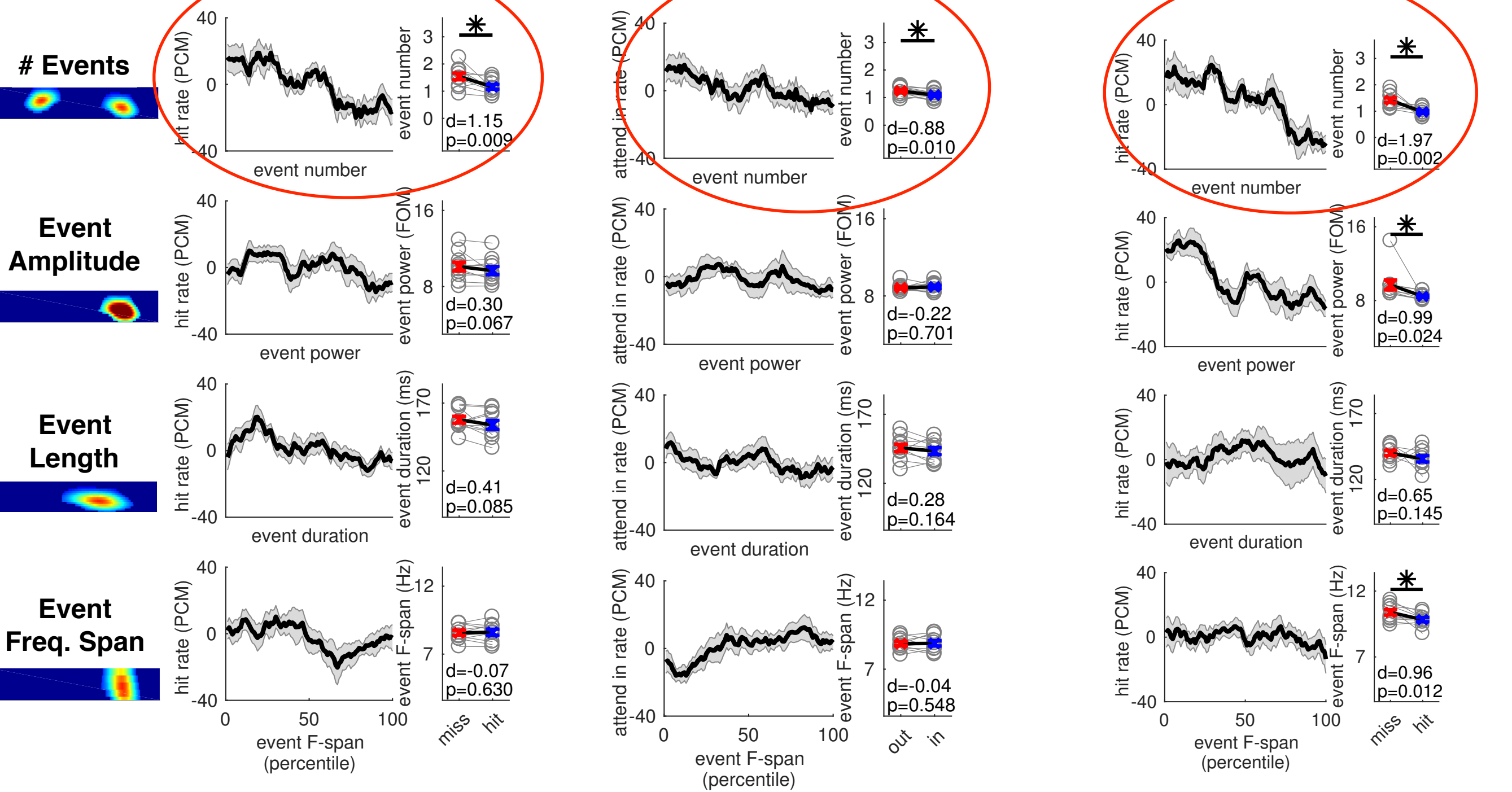
Number of Beta Events is Higher in Non-Detected / Non-Attended Trials



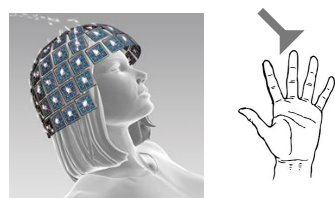
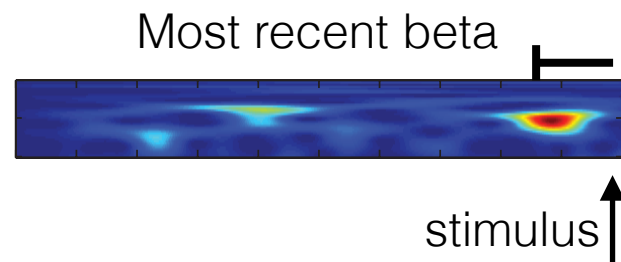
Human Detection Task

Human Attention Task

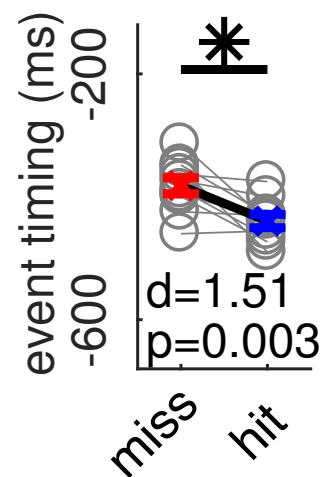
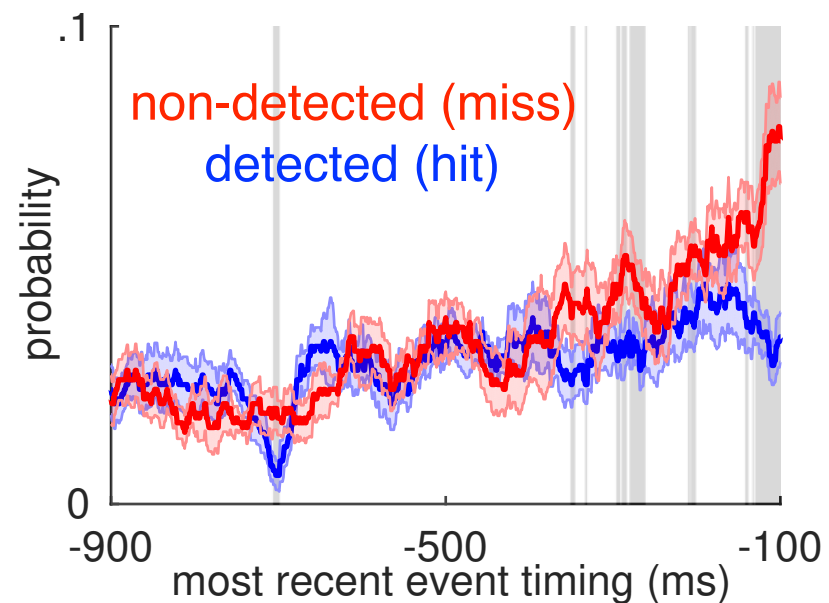
Mouse Detection Task



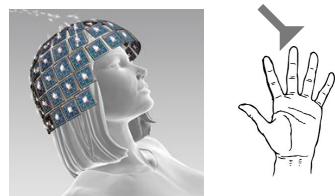
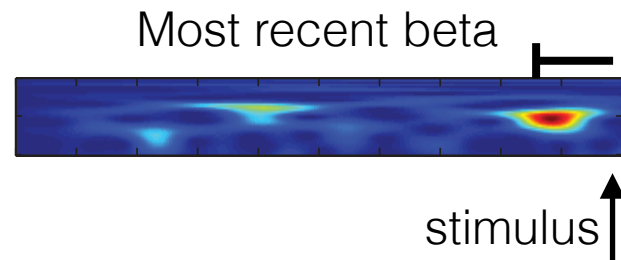
Non-Detected Stimuli have More Recent Prestimulus Beta Events than Detected Stimuli



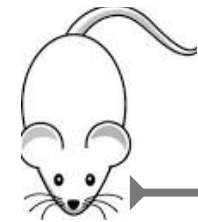
Human Detection Task



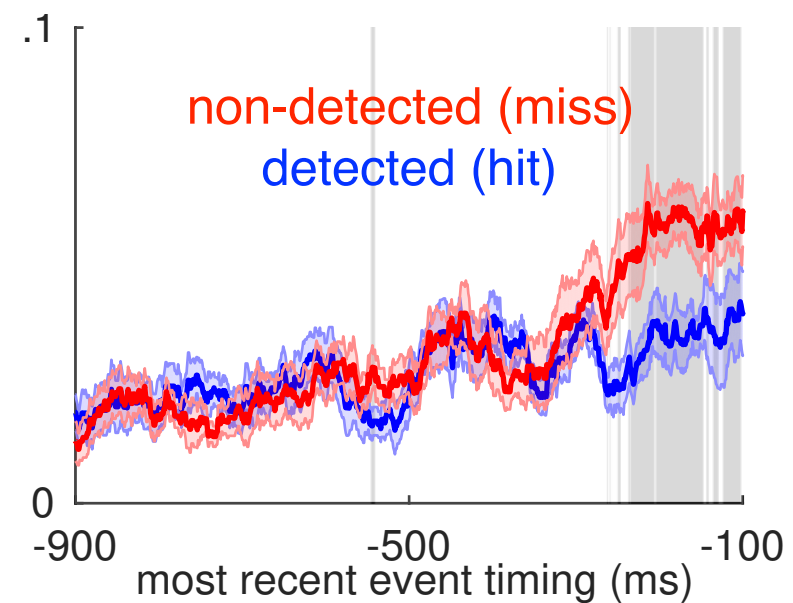
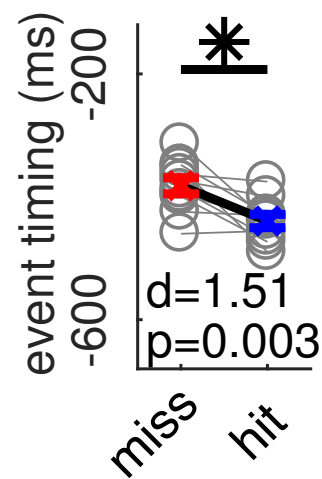
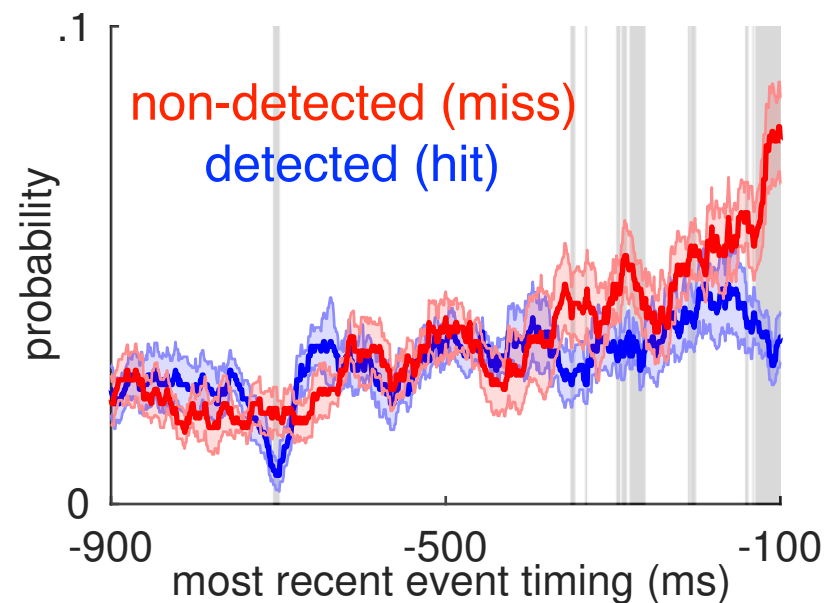
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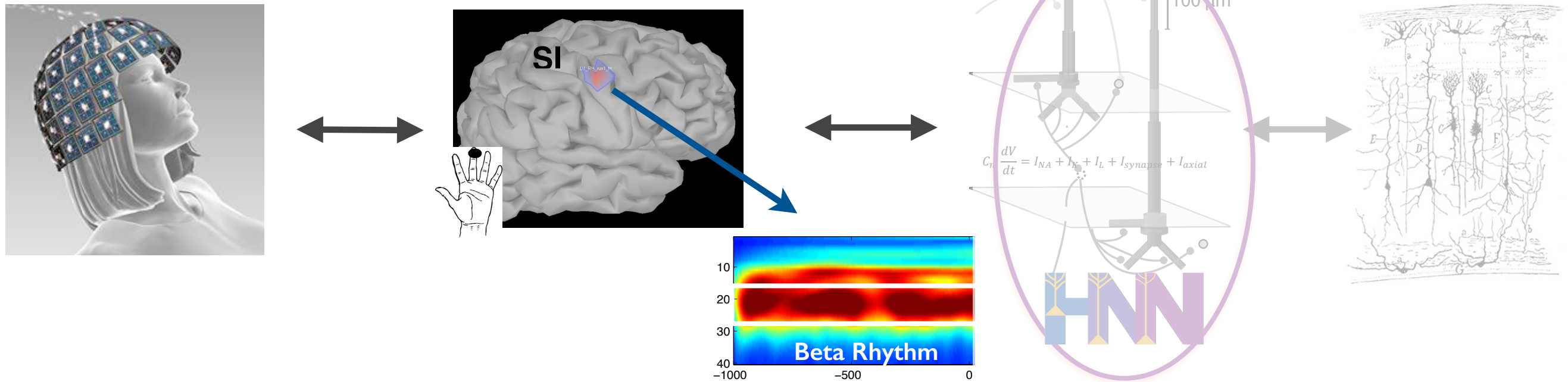


Human Detection Task



Mouse Detection Task





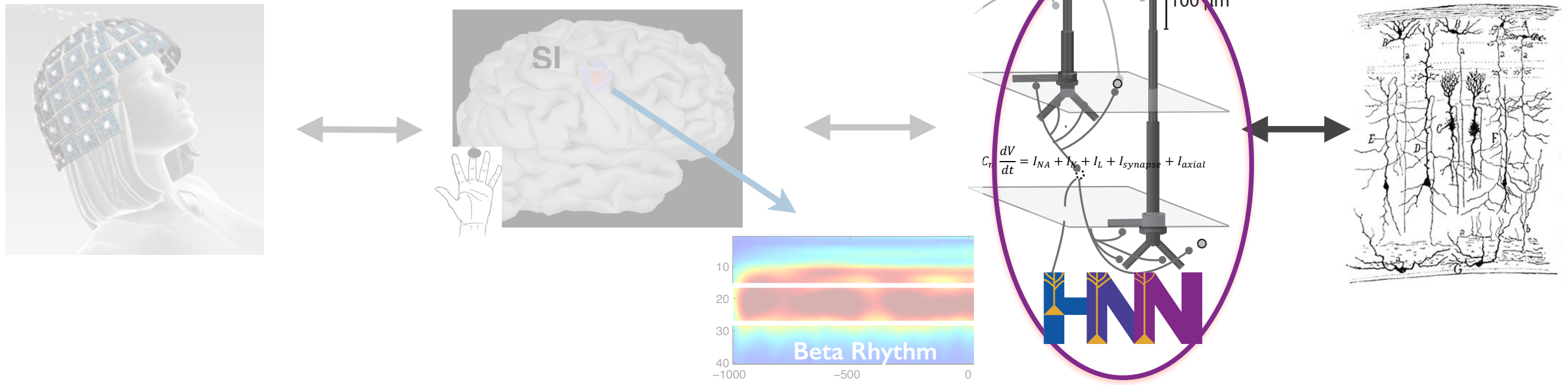
Applying HNN to study mechanisms by which beta inhibits perception

What does beta look like in unaveraged data?

Beta “events” are transient (<150ms) with a stereotypical waveform.

What features underly functionally relevant differences in average power?

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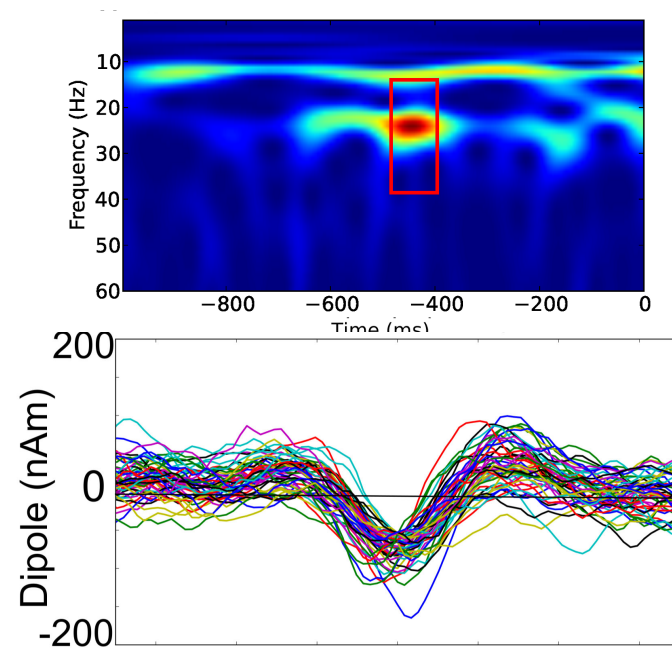
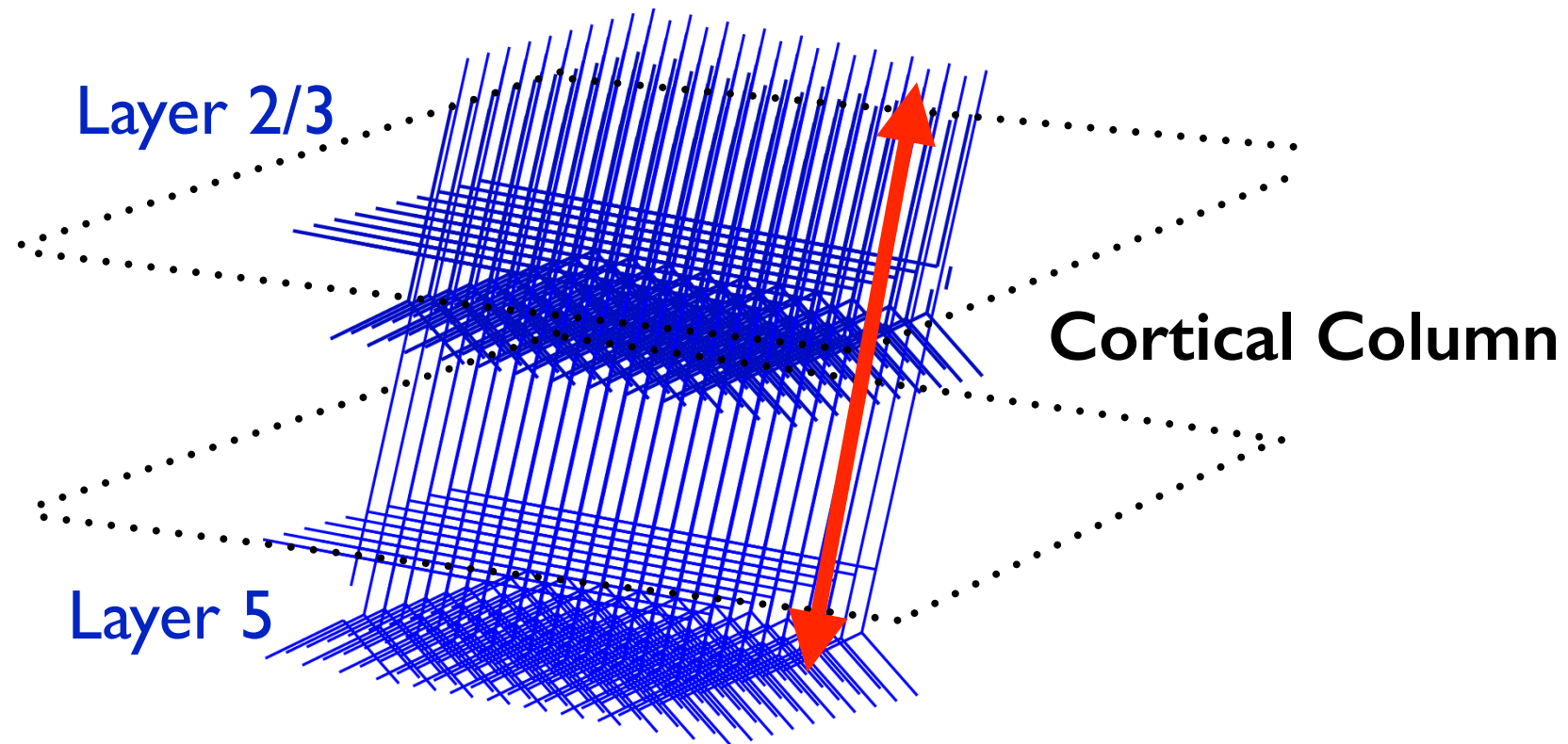
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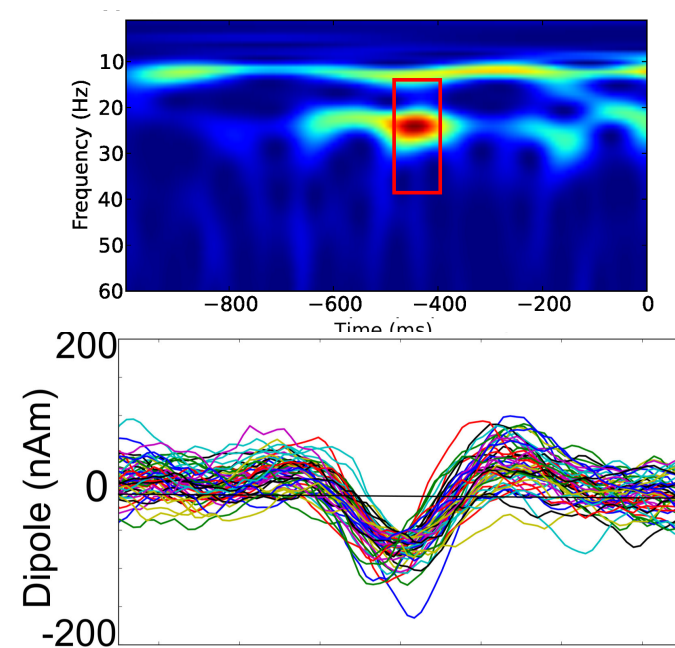
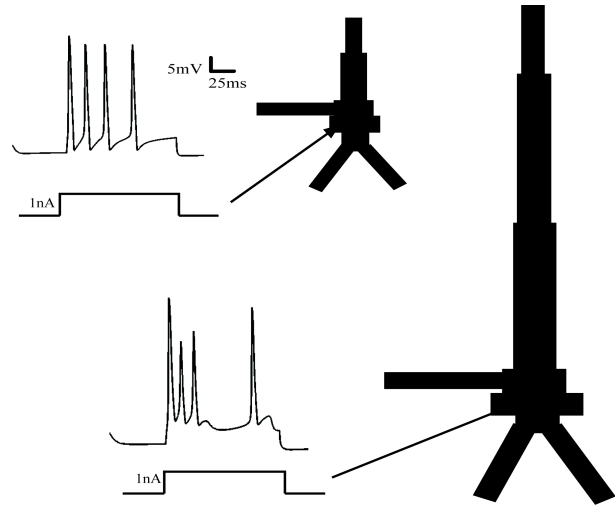
What are the circuit mechanisms underlying these differences?

Using HNN to Simulate Macroscale Beta “Events”



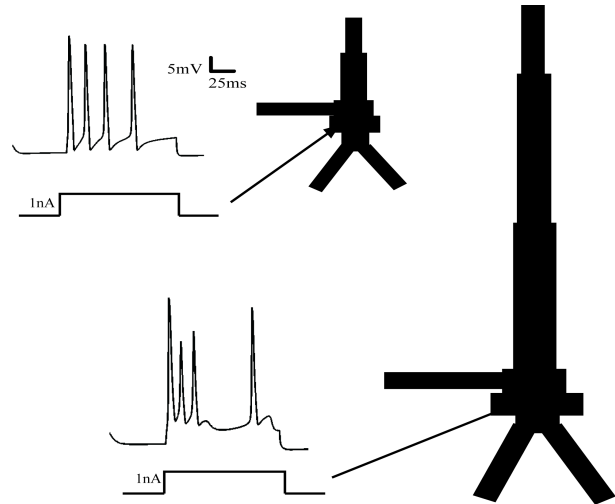
Using HNN to Simulate Macroscale Beta “Events”

Fix Cellular Physiology

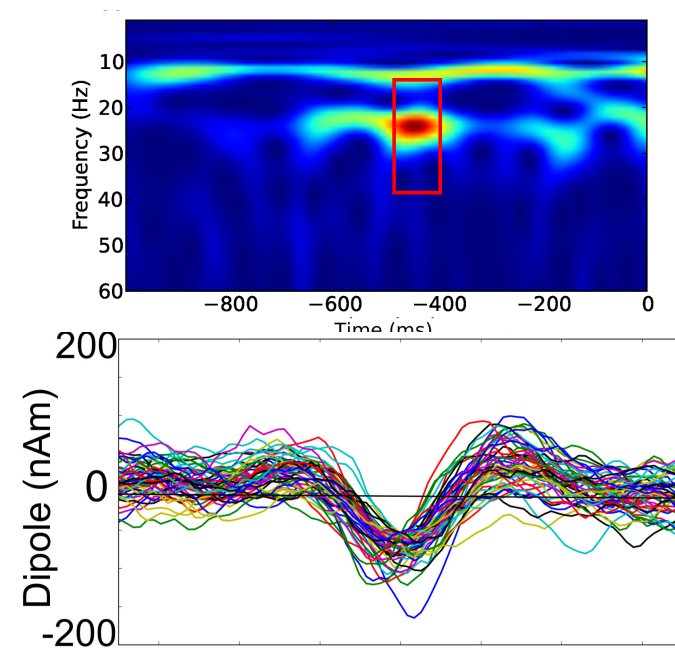
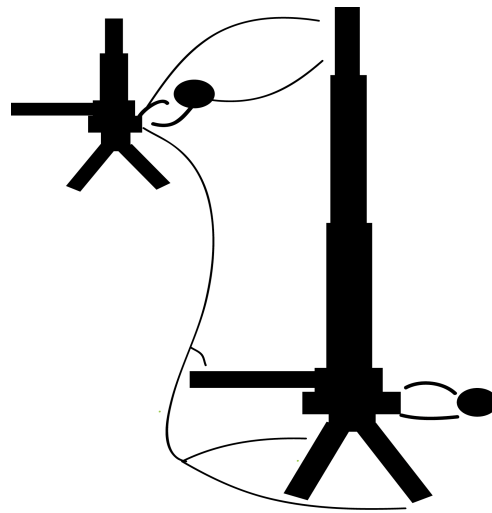


Using HNN to Simulate Macroscale Beta “Events”

Fix Cellular Physiology

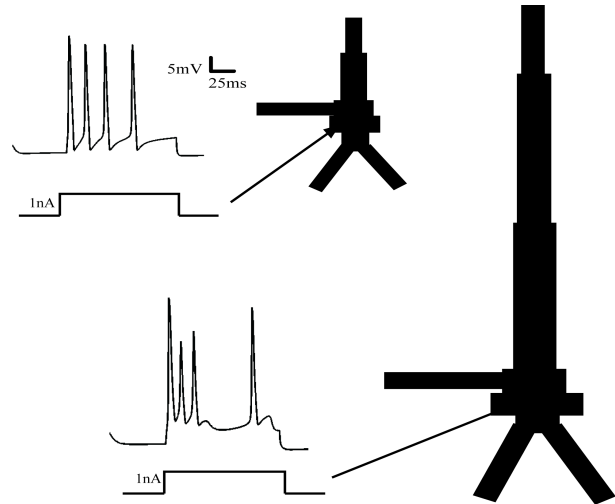


Fix Local Network Connectivity

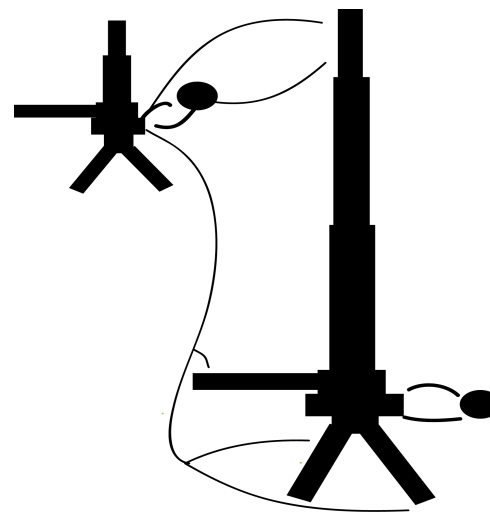


Using HNN to Simulate Macroscale Beta “Events”

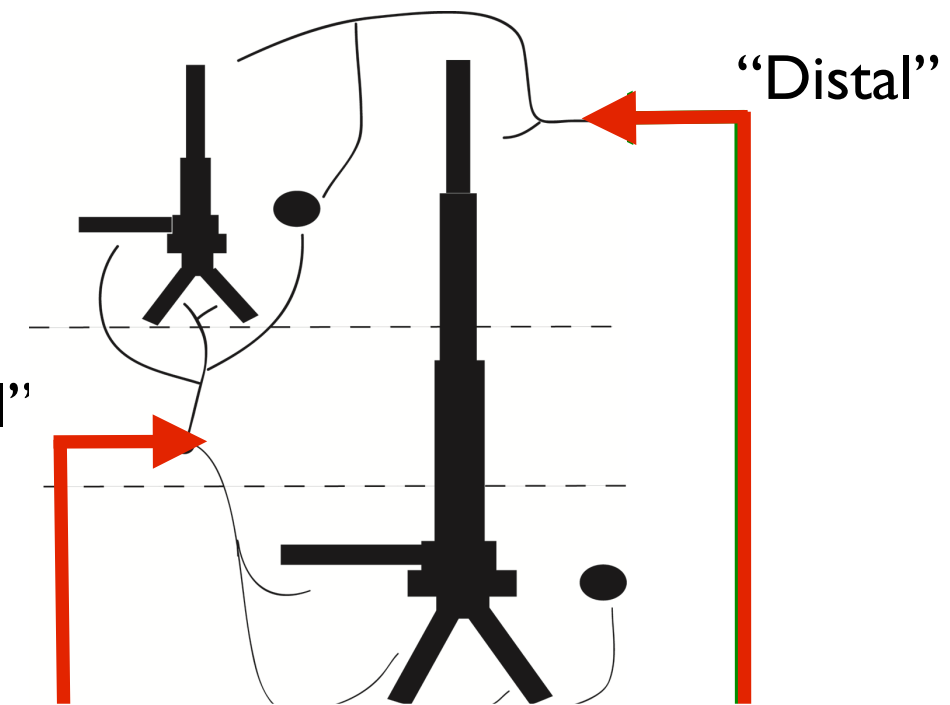
Fix Cellular Physiology



Fix Local Network Connectivity



Exogenous “Proximal” & “Distal” Excitatory Synaptic Drive



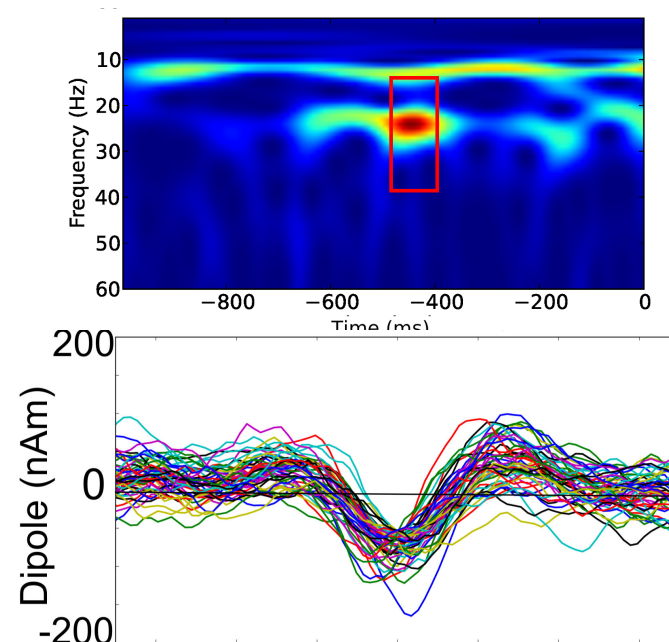
Timing



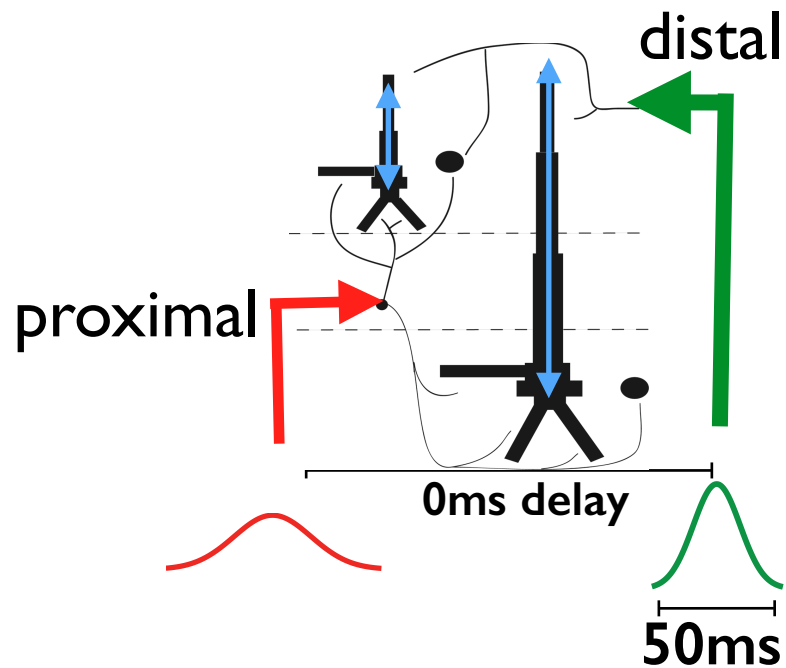
Strength

Vary Parameters of Drive

- sources of drive modeled a spike train generators

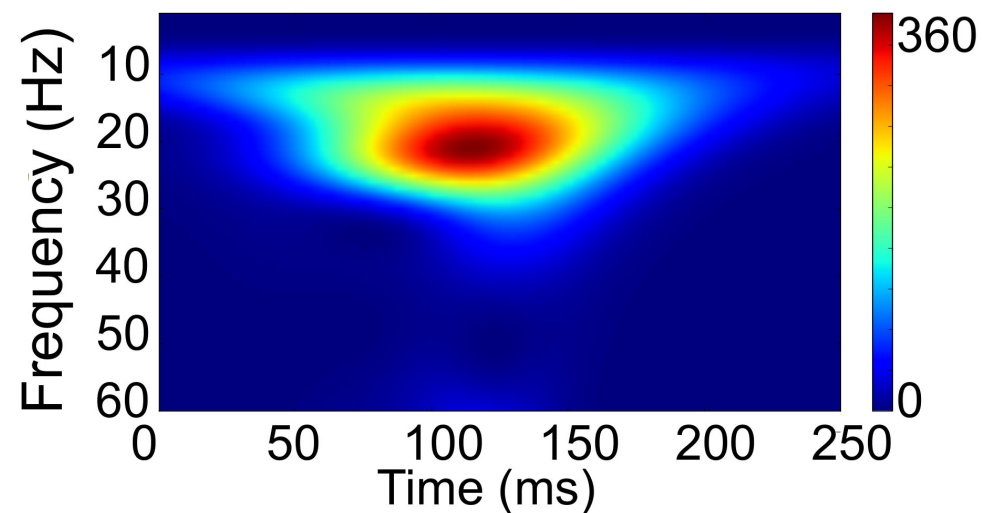
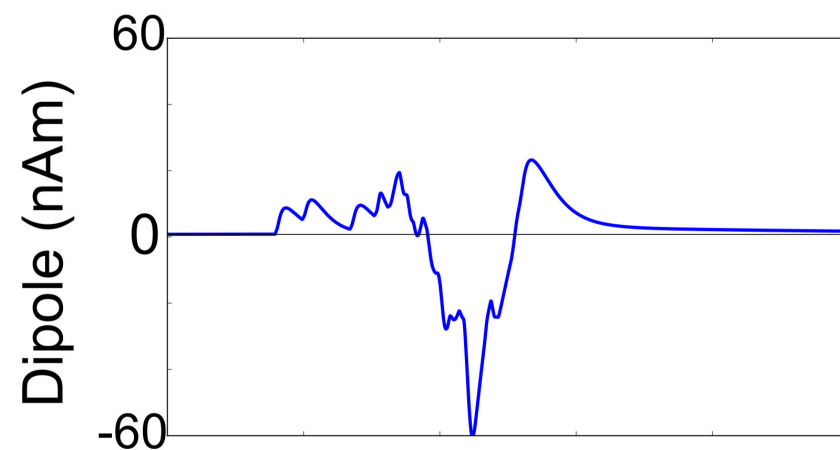


HNN Model Prediction

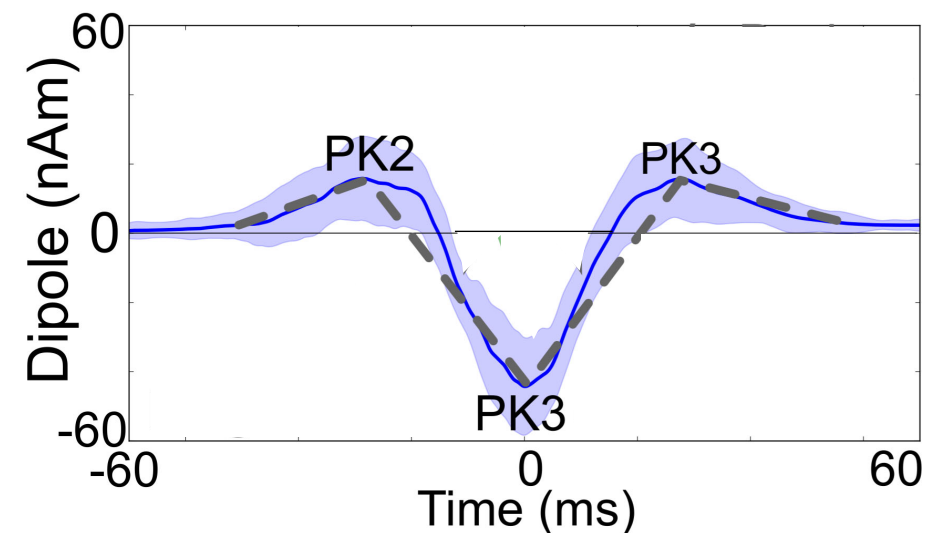
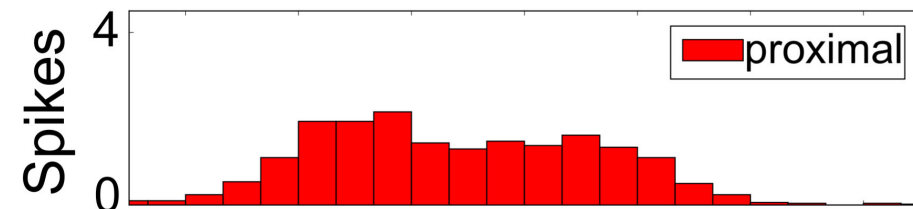
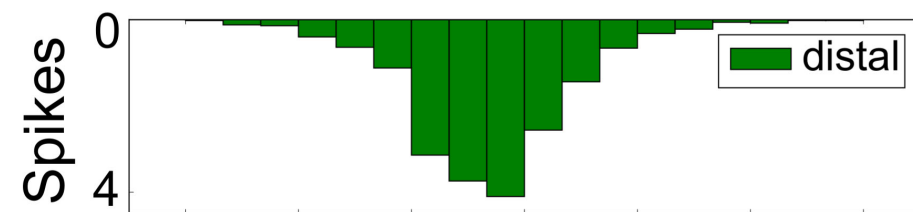


Beta “Event” Mechanism:

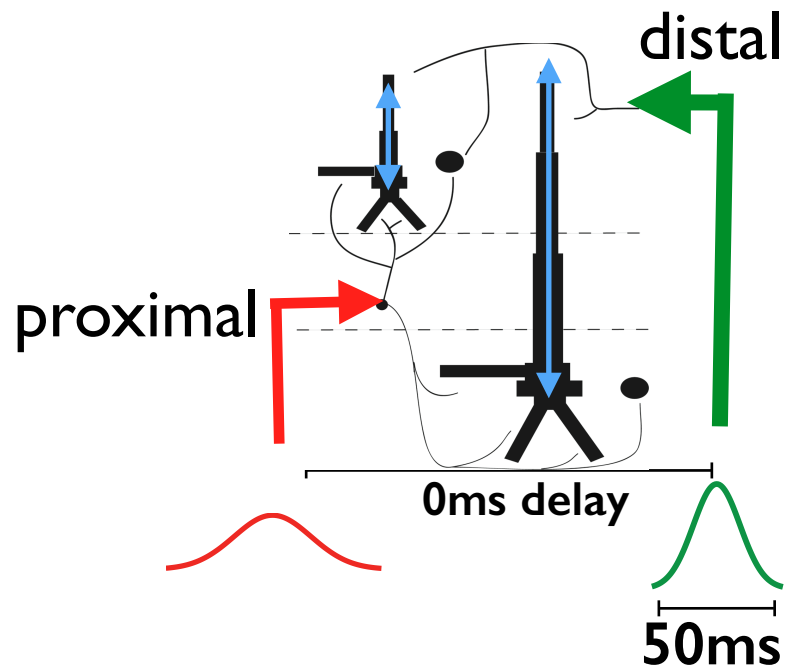
Beta events emerge from a broad proximal excitatory synaptic drive simultaneous with a strong distal drive that lasts a beta period (~50ms).



Avg. 50 Beta Events

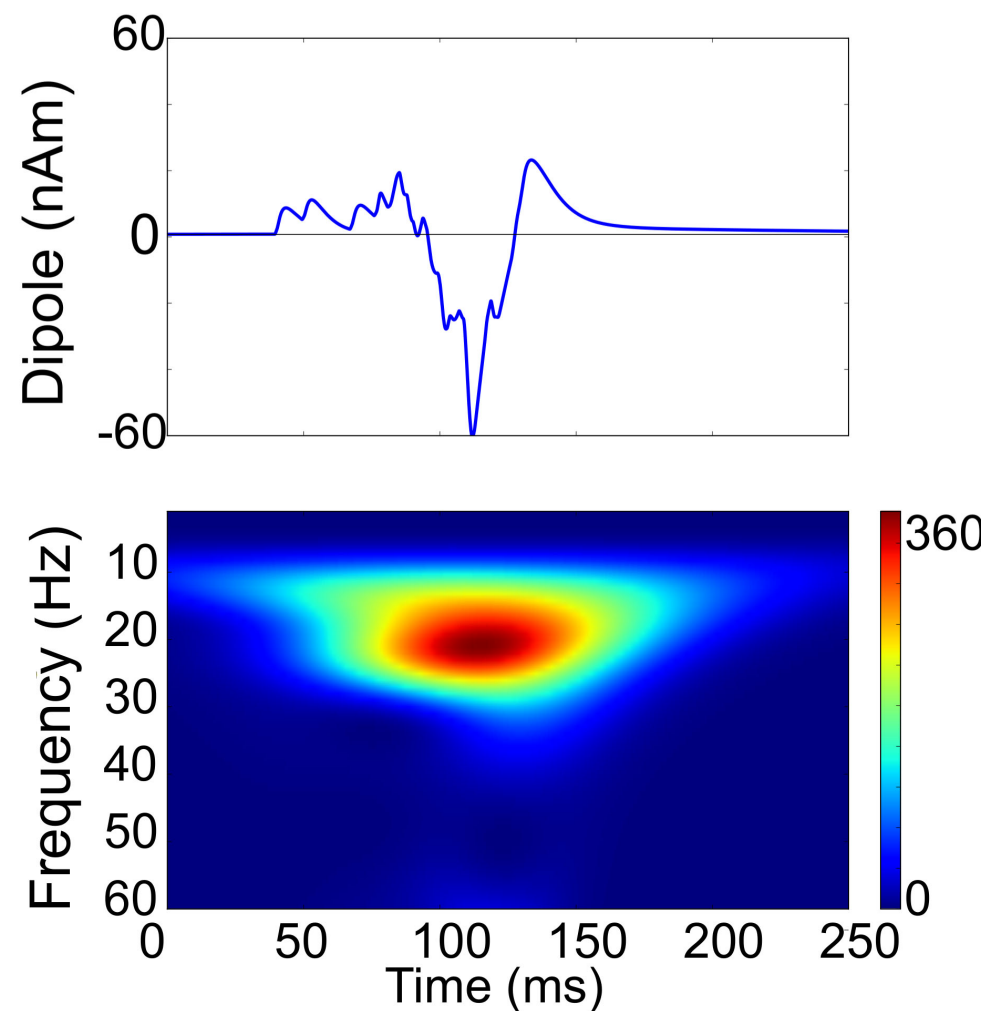


HNN Model Prediction

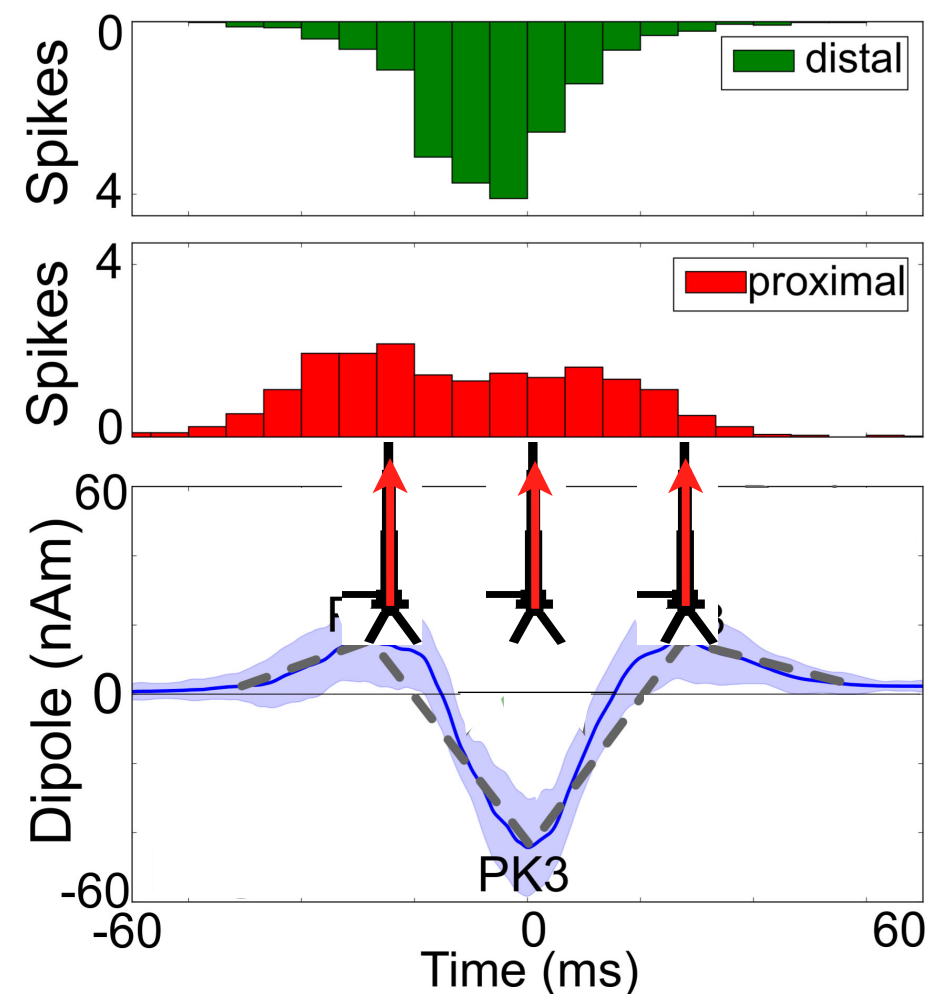


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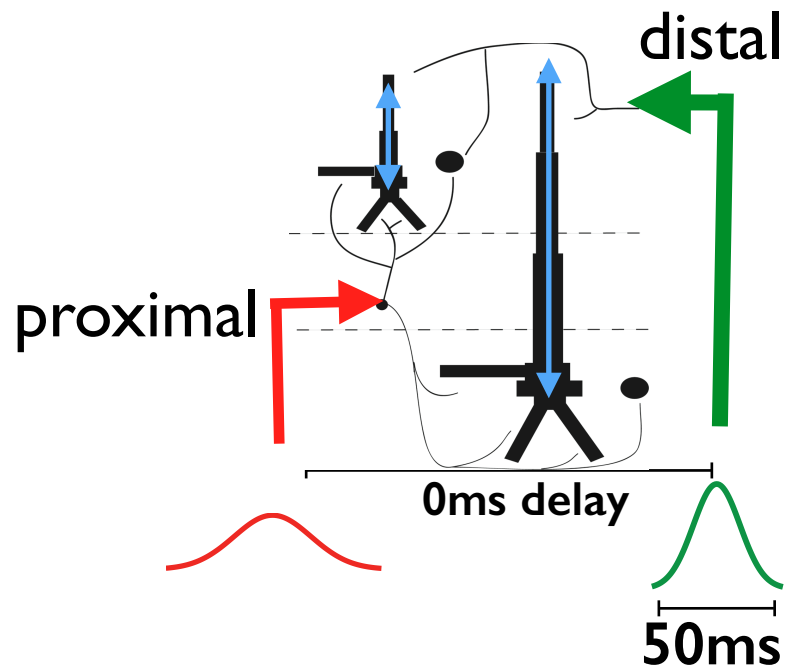
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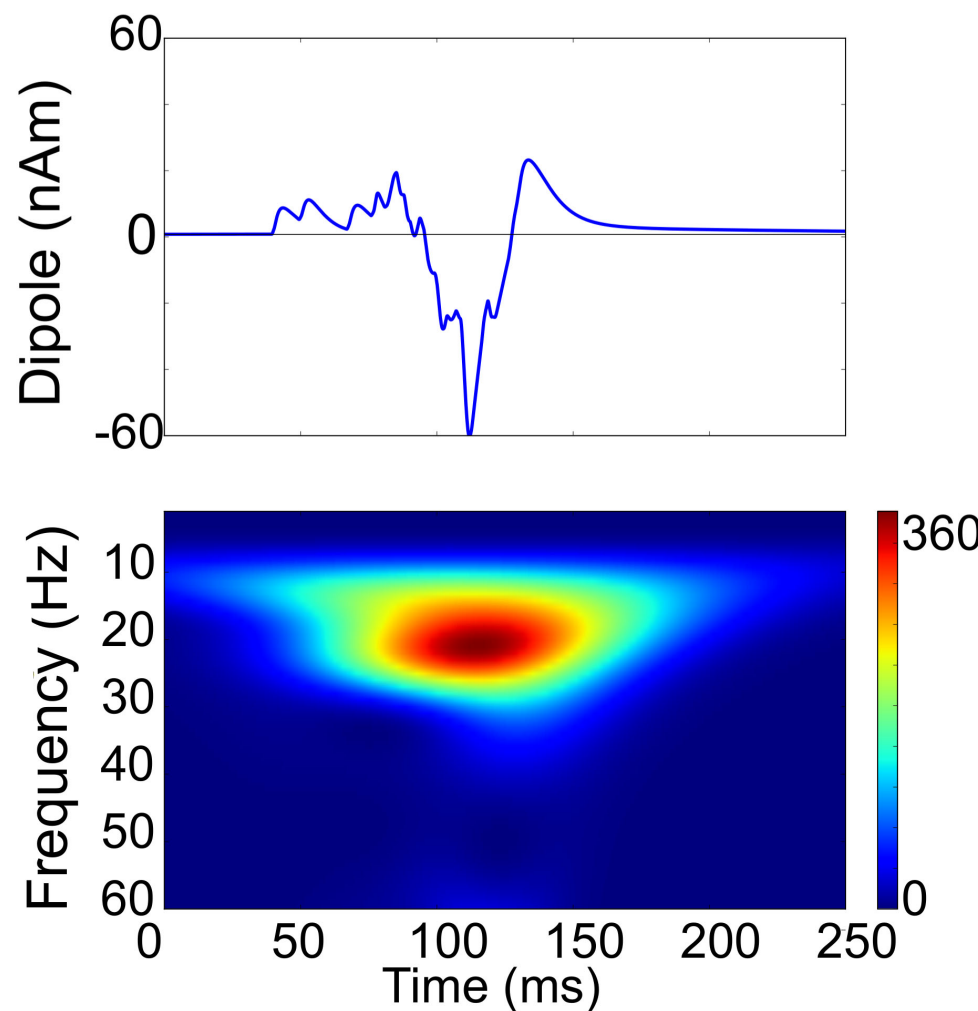


HNN Model Prediction

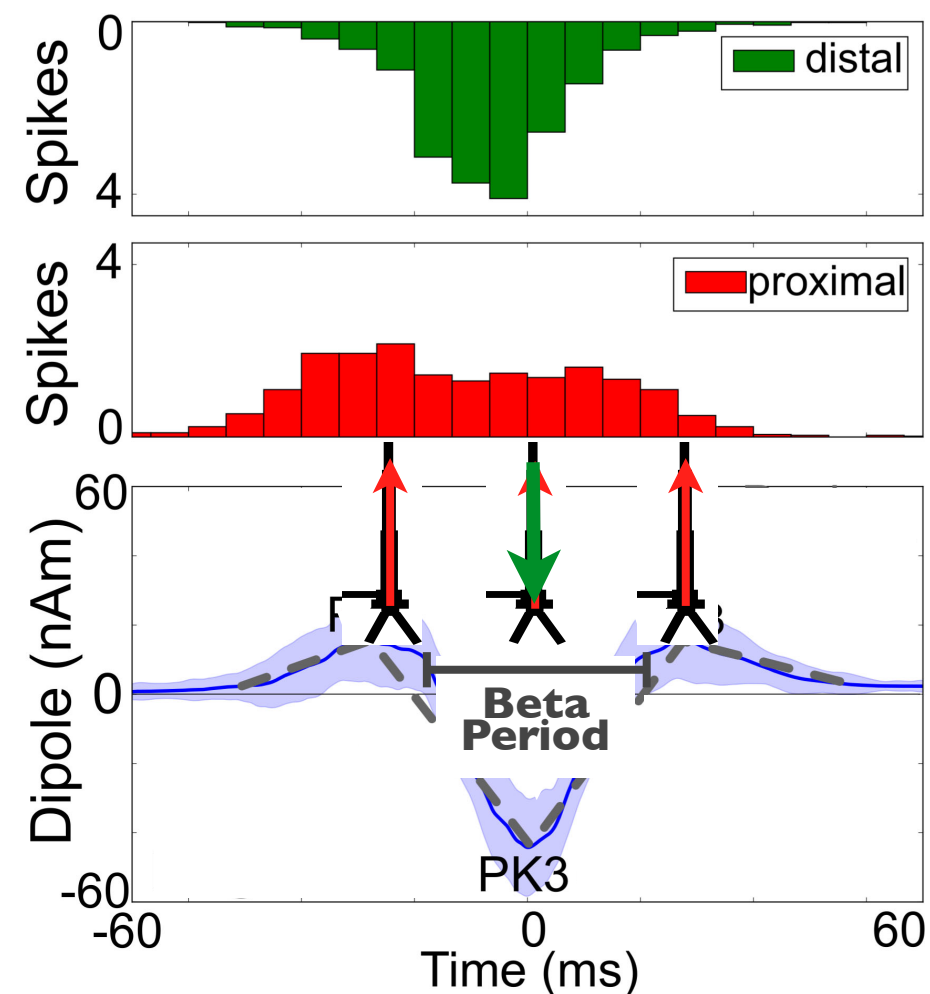


Beta “Event” Mechanism:

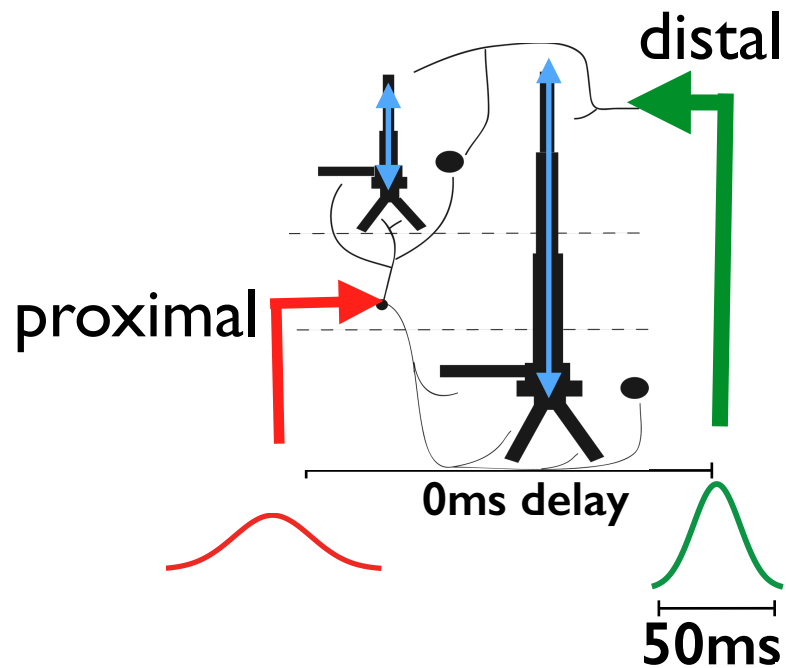
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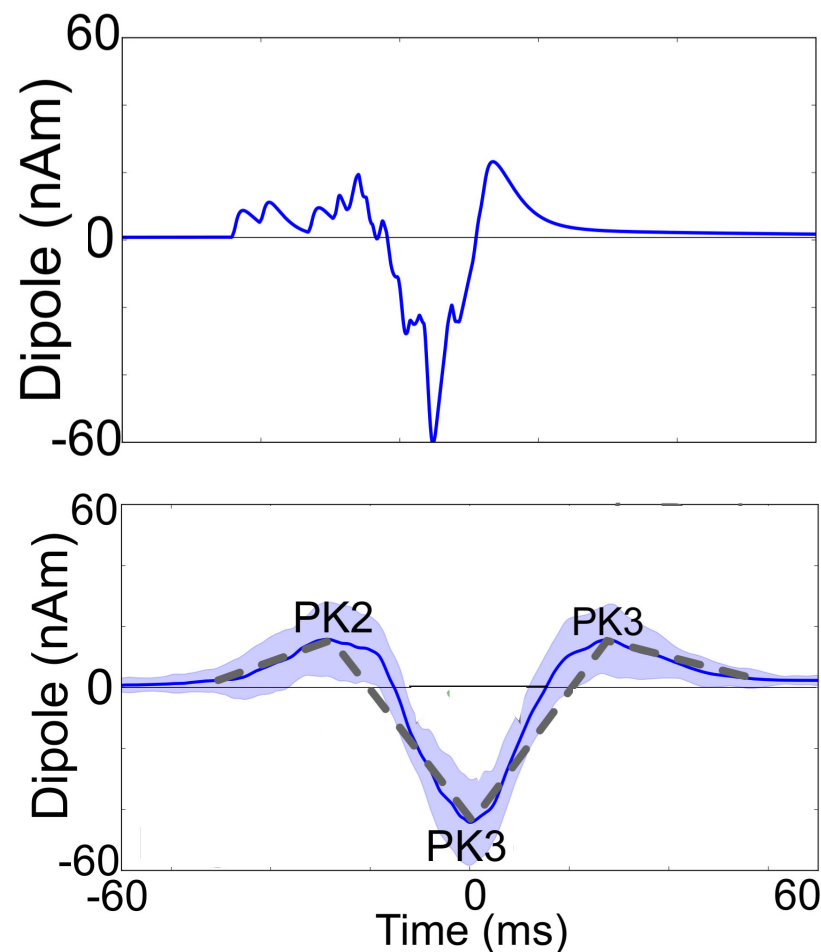
HNN Model Prediction



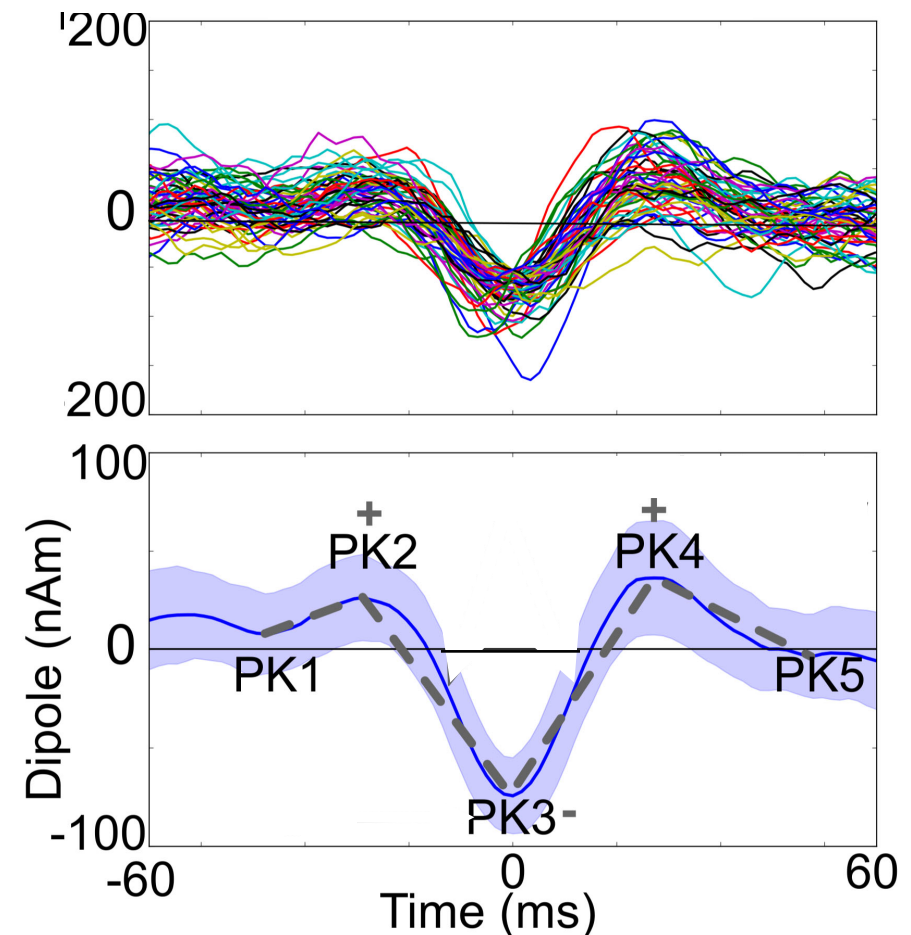
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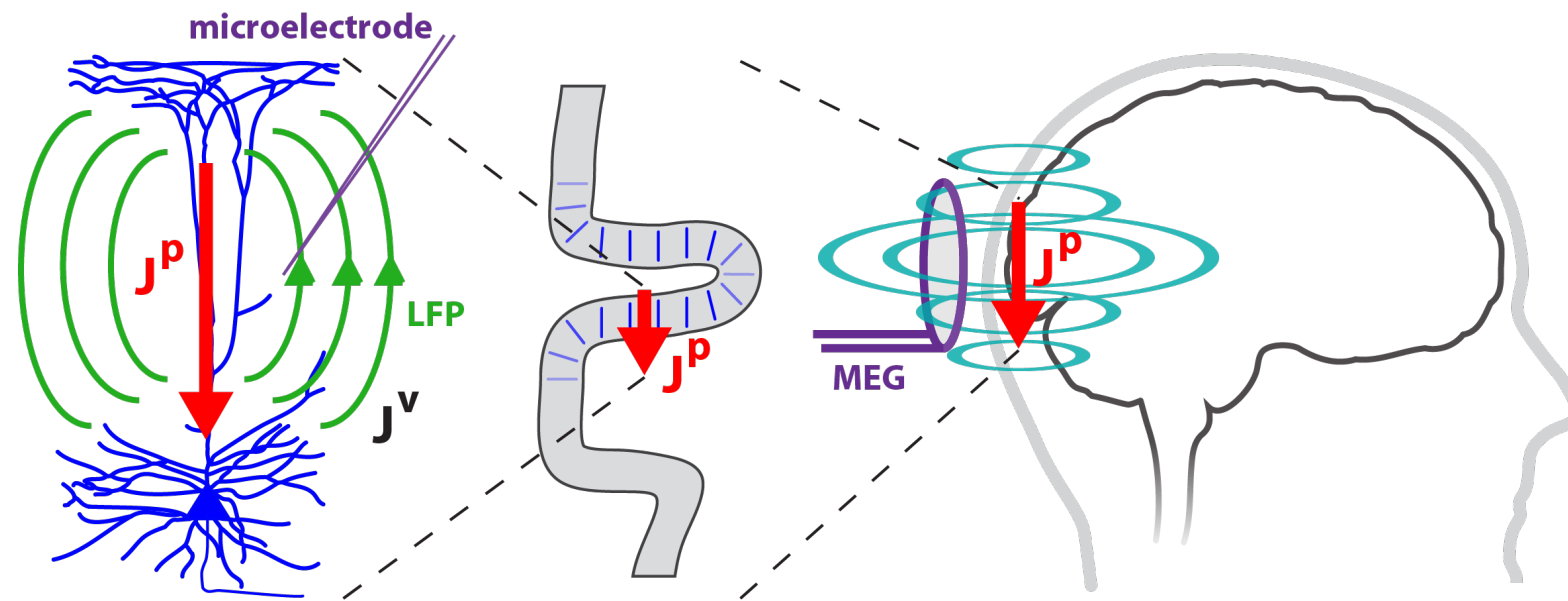
Model Data



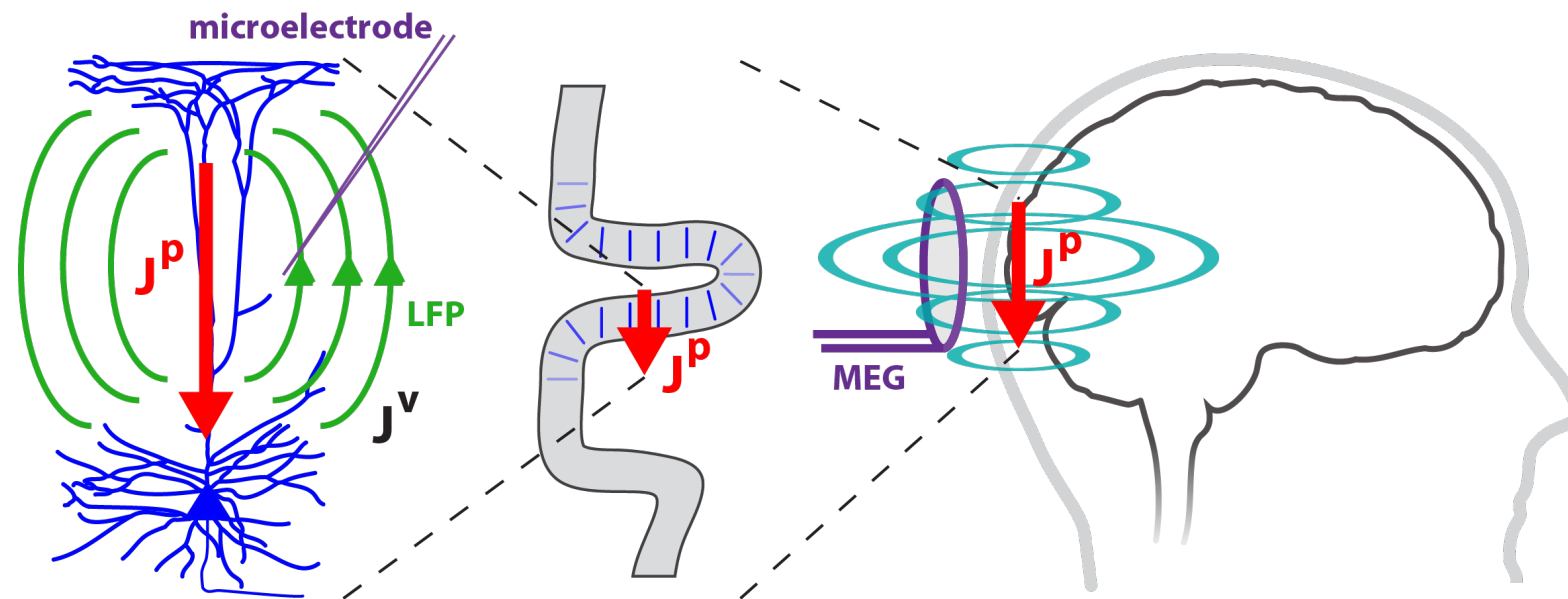
MEG Data



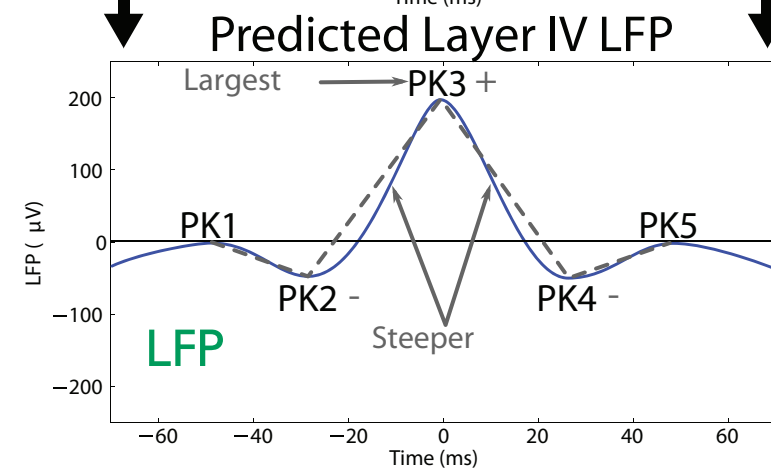
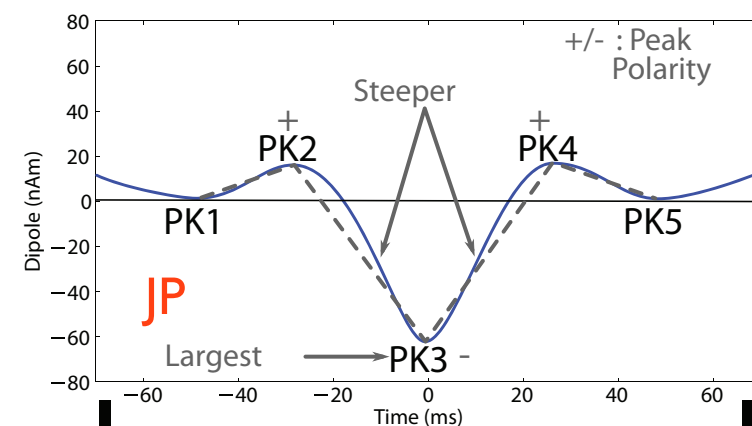
Testing Model Predictions with Invasive Recordings



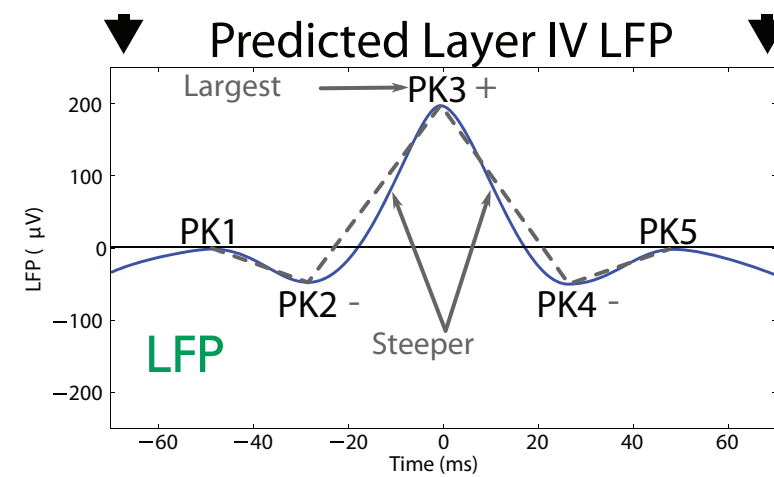
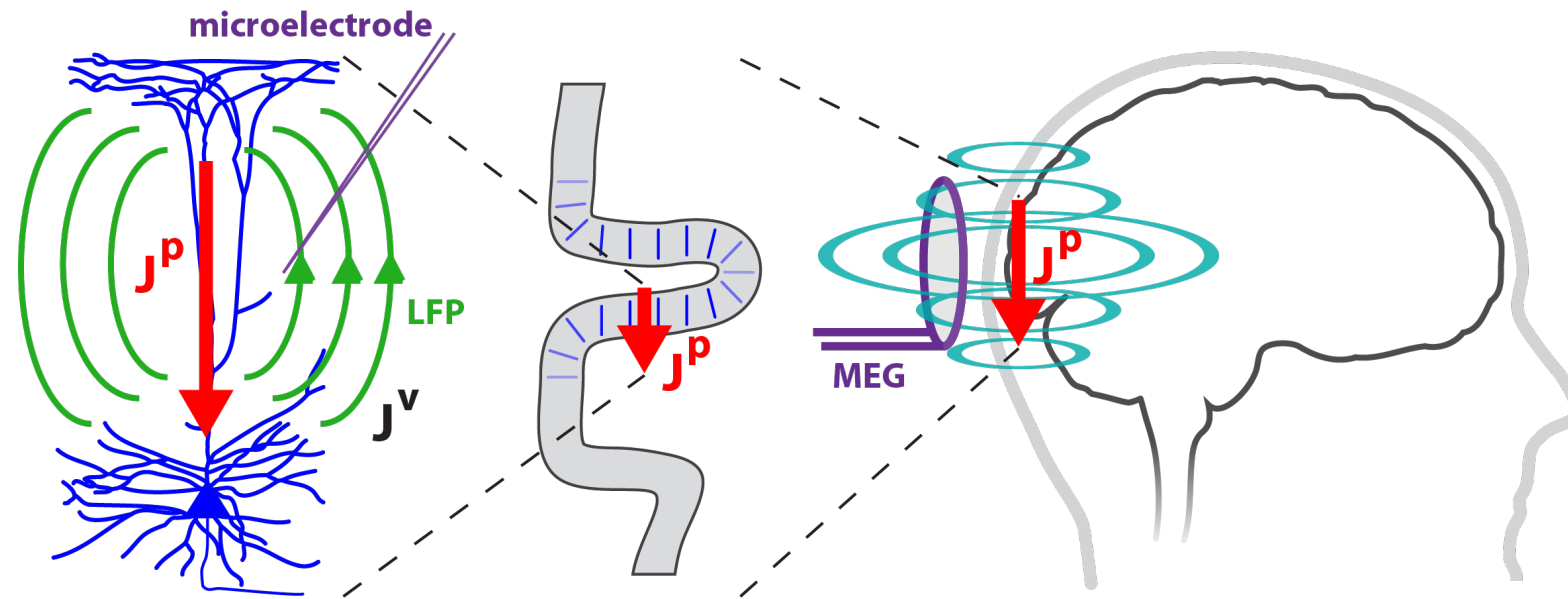
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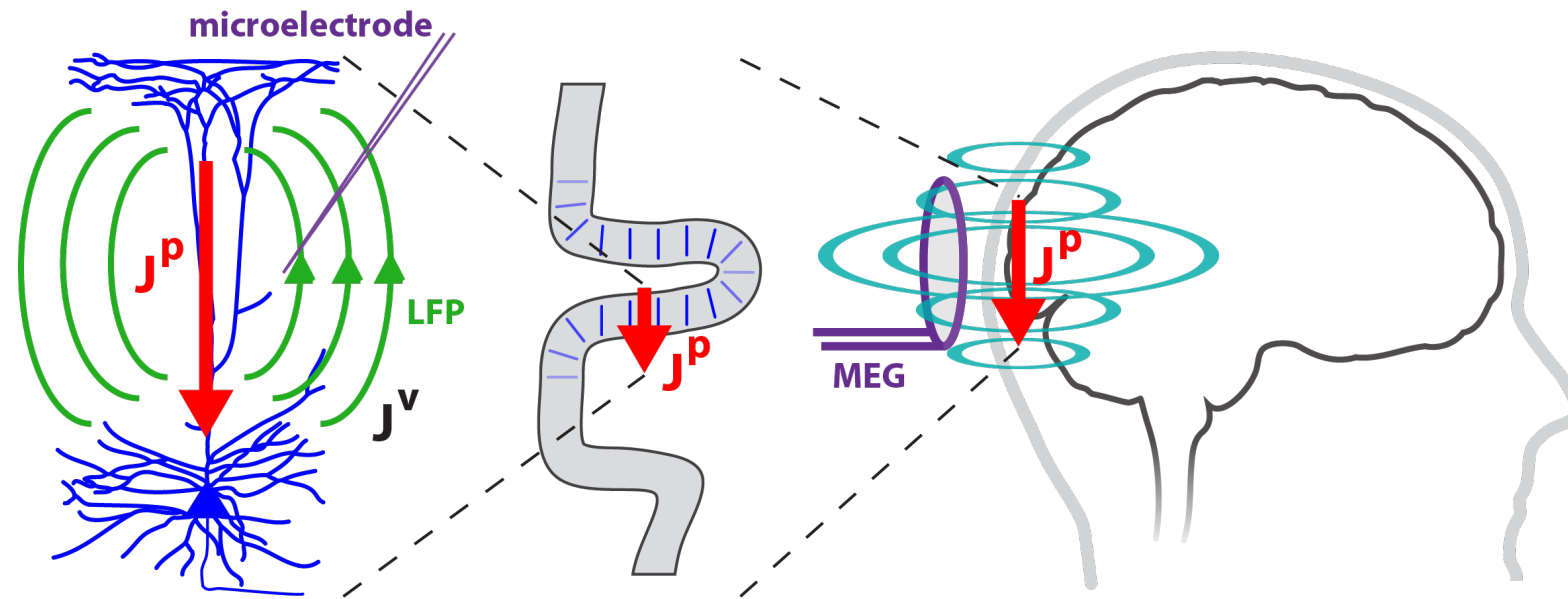
Primary Current Dipole



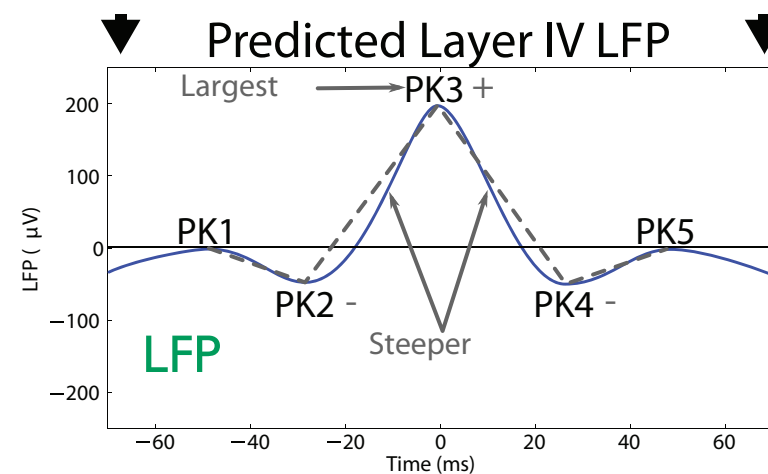
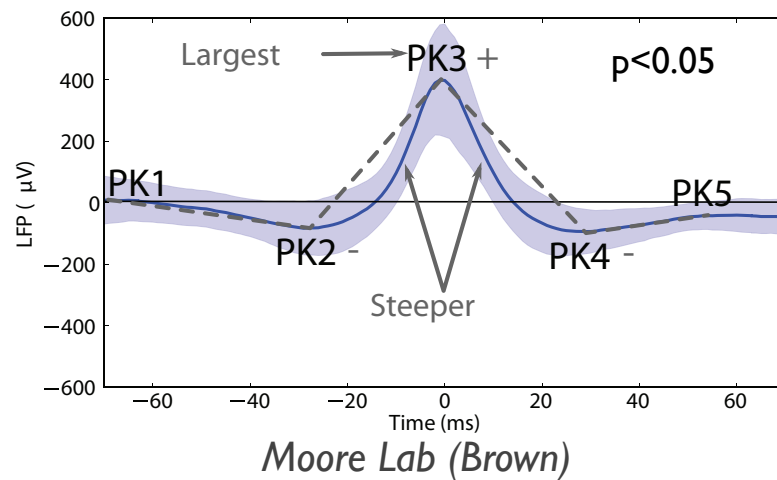
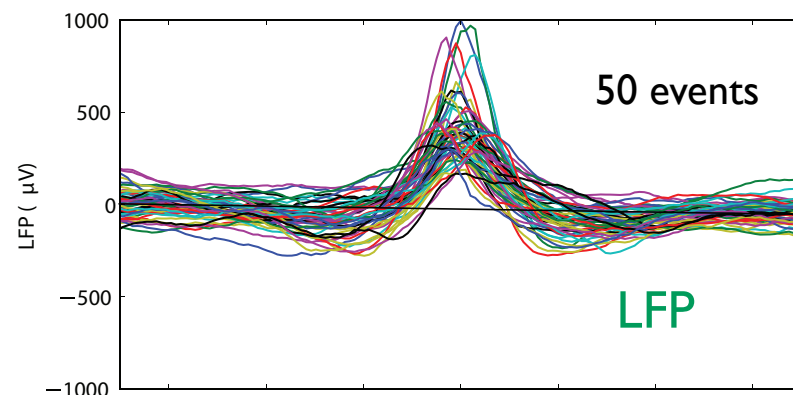
Testing Model Predictions with Invasive Recordings



Testing Model Predictions with Invasive Recordings

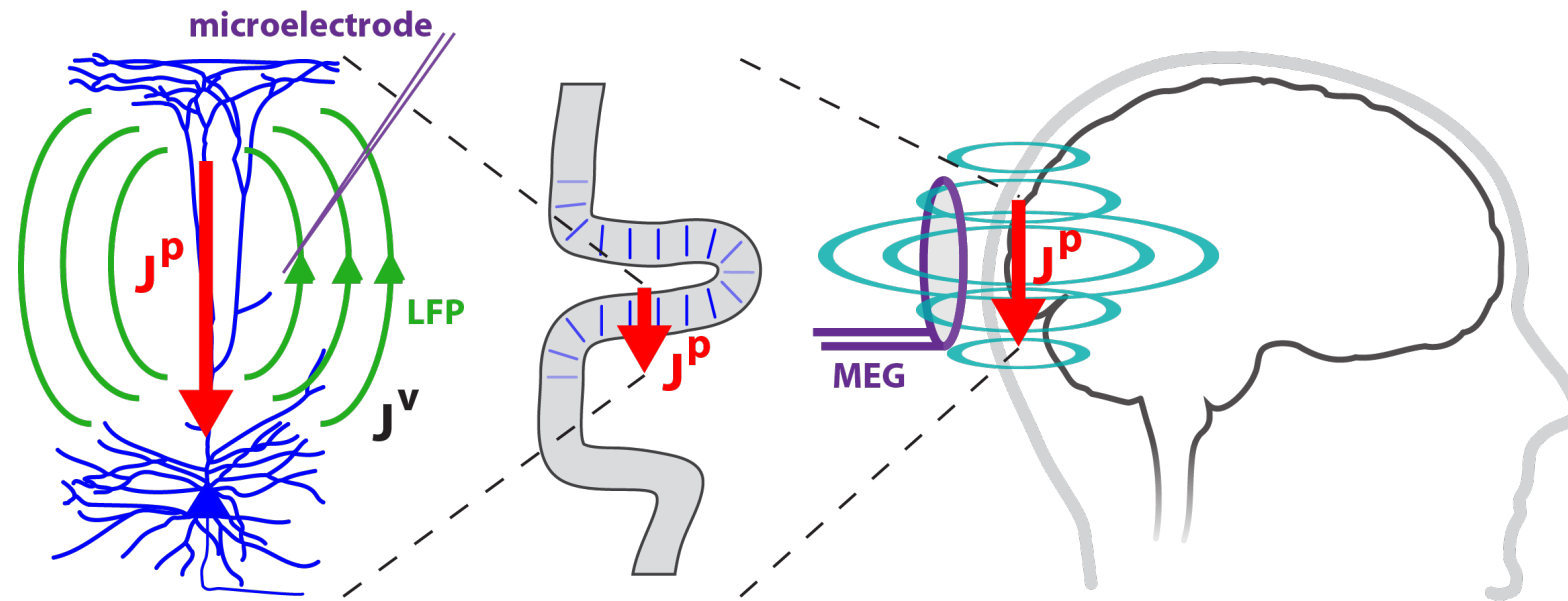


Anesthetized Mouse Layer IV LFP Beta “Events”

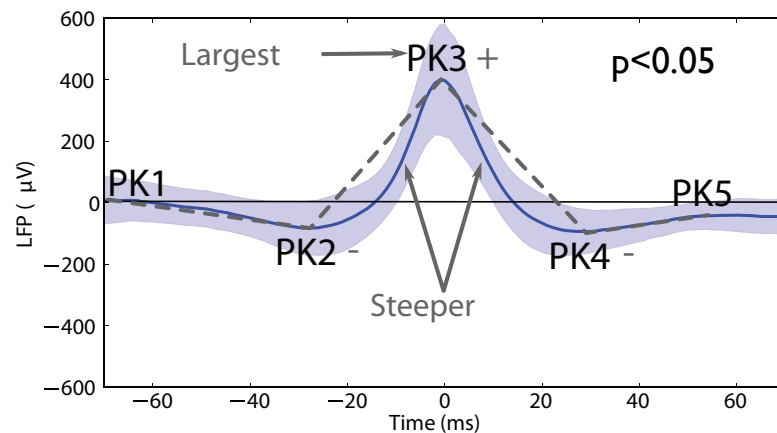
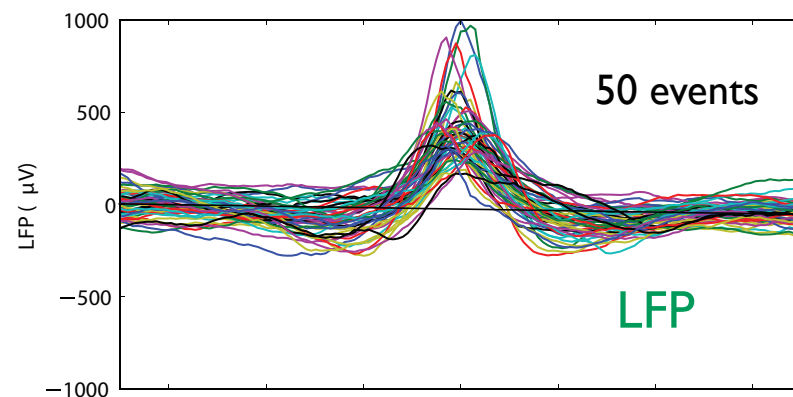


Beta event waveform is consistent across recording modalities and species.

Testing Model Predictions with Invasive Recordings

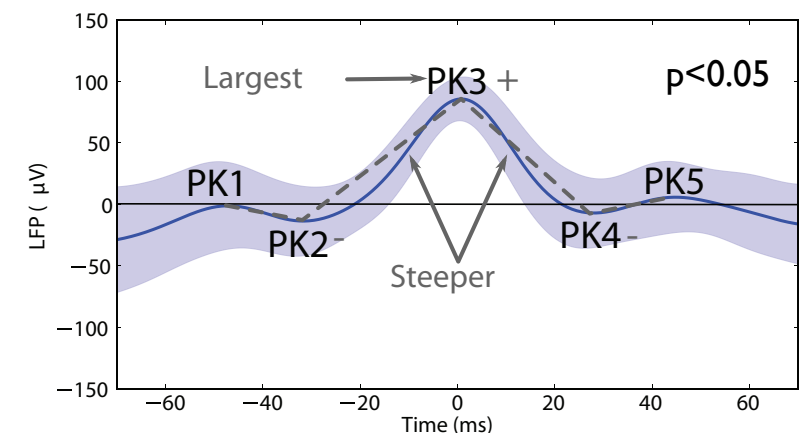
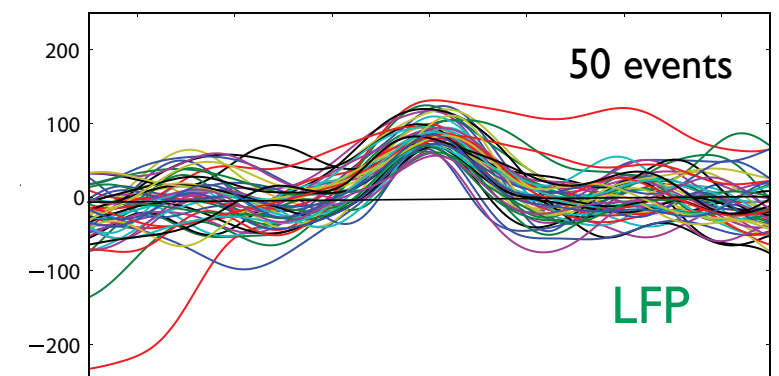


Anesthetized Mouse Layer IV
LFP Beta “Events”



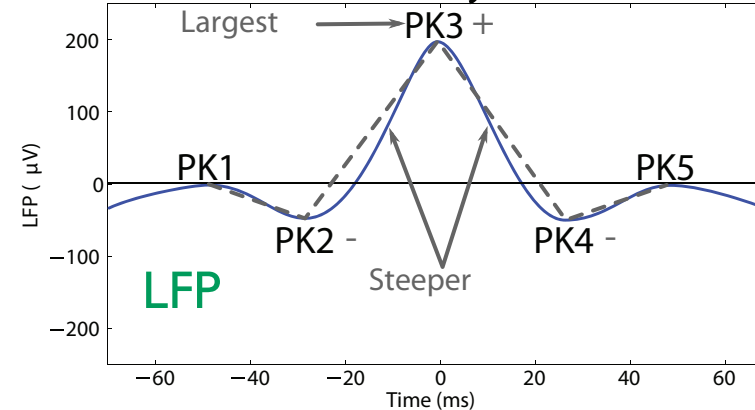
Moore Lab (Brown)

Awake Monkey Layer IV
LFP Beta “Events”



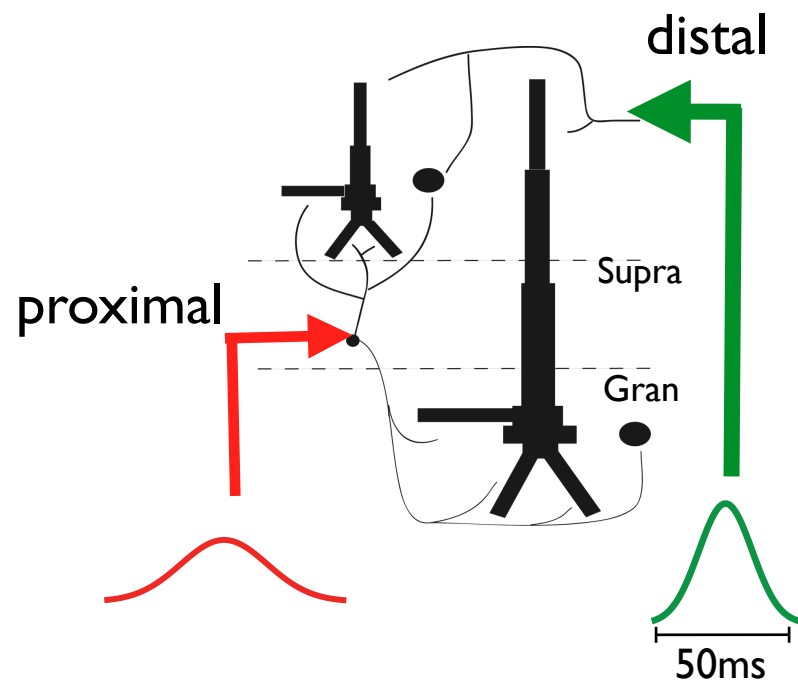
Schroeder Lab (Nathan Kline Inst.)
Saskia Haegens

Predicted Layer IV LFP



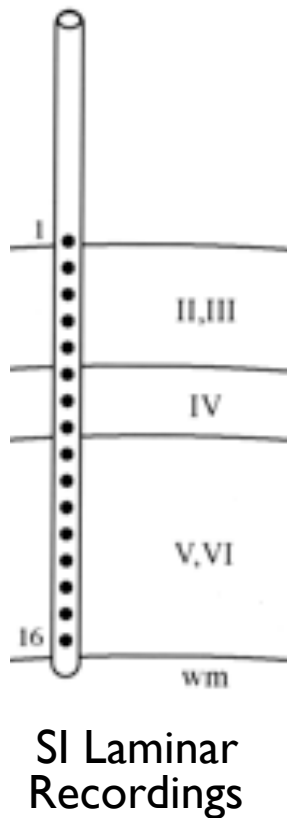
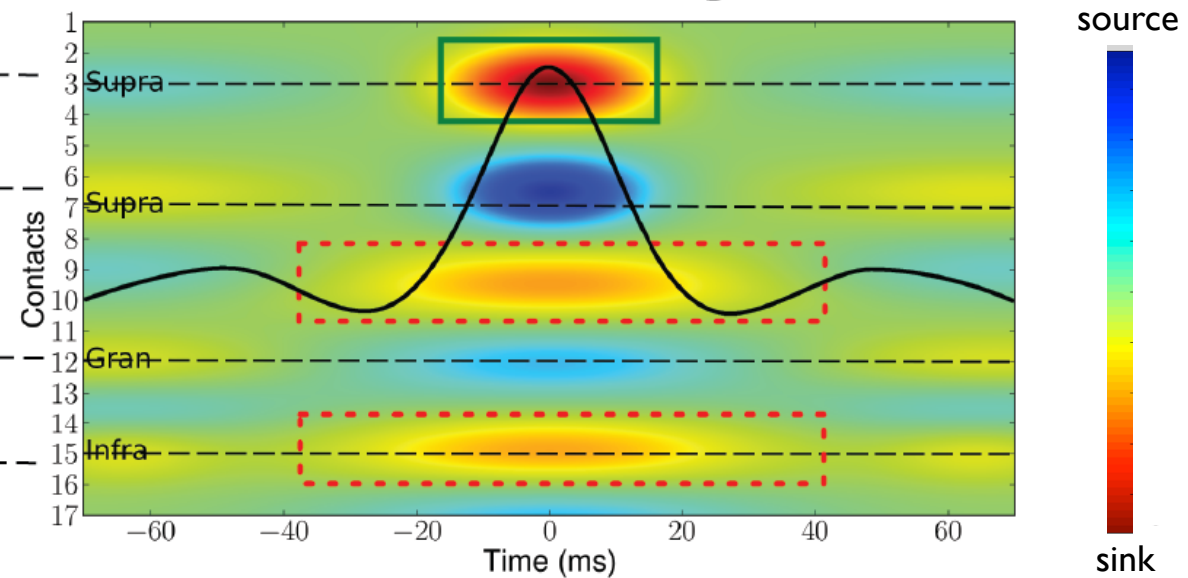
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Testing Model Predictions with Invasive Recordings

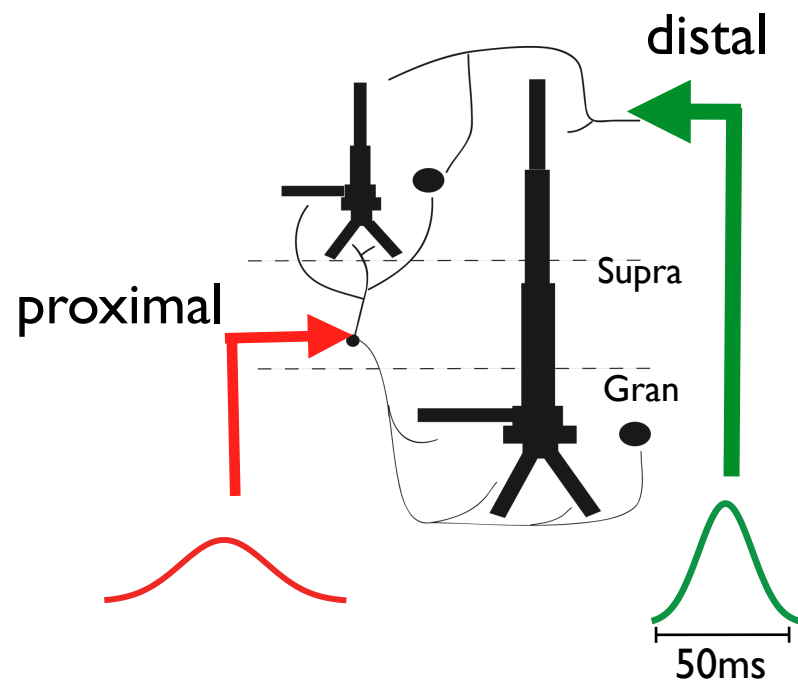


Beta events emerge from a broad proximal synaptic drive simultaneous with a strong ~50ms distal drive

Predicted CSD During Beta Event

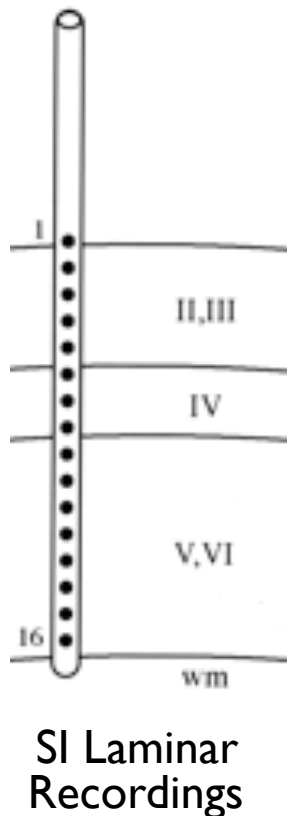
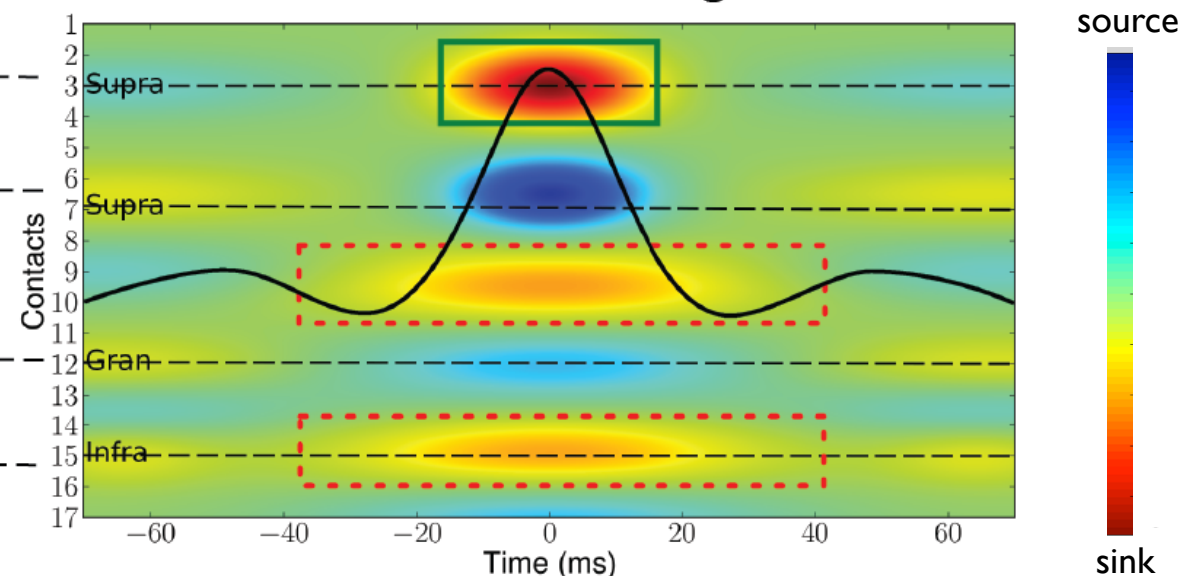


Testing Model Predictions with Invasive Recordings

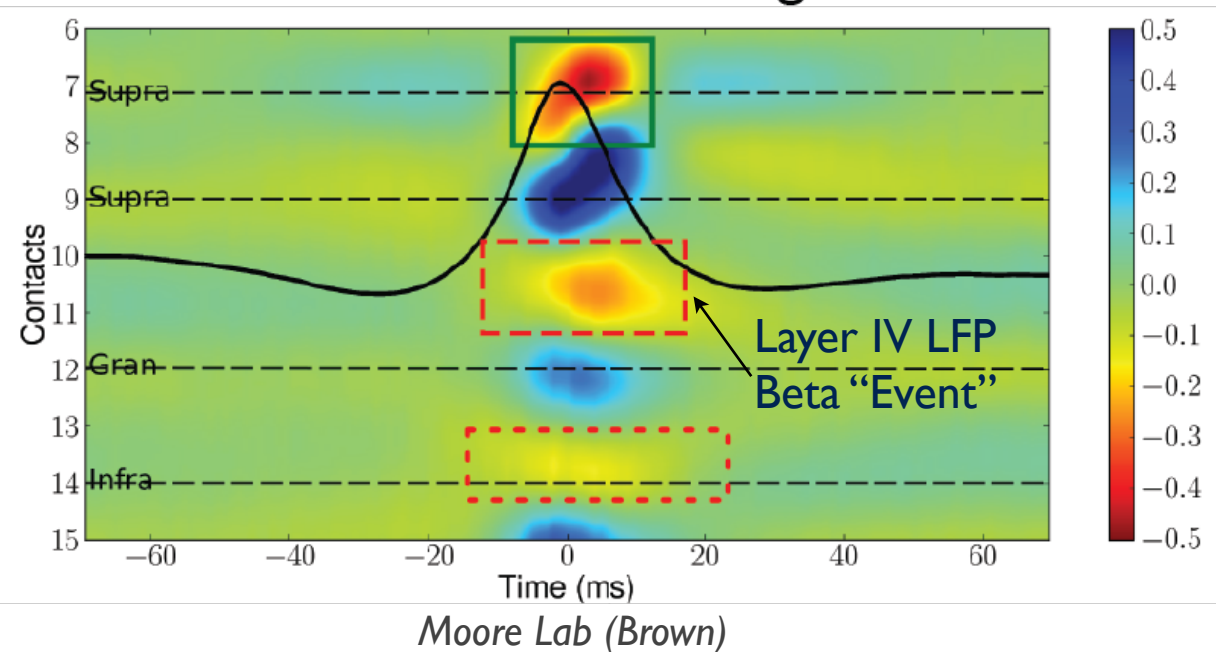


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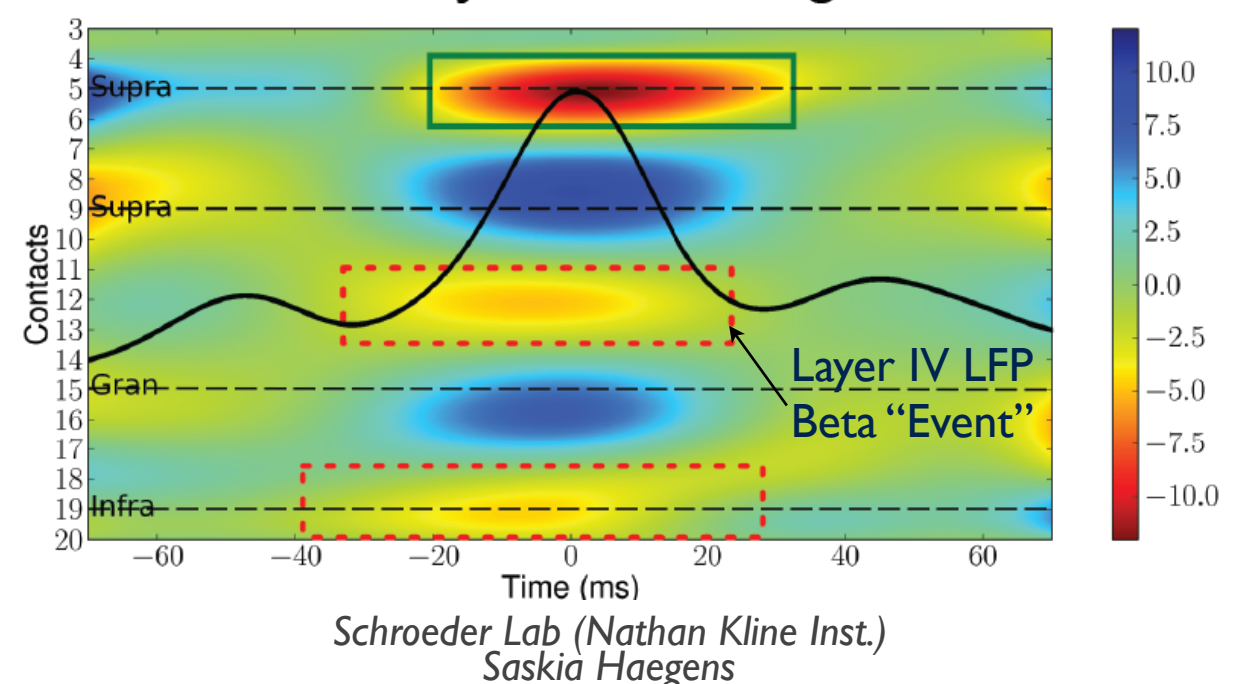
Predicted CSD During Beta Event

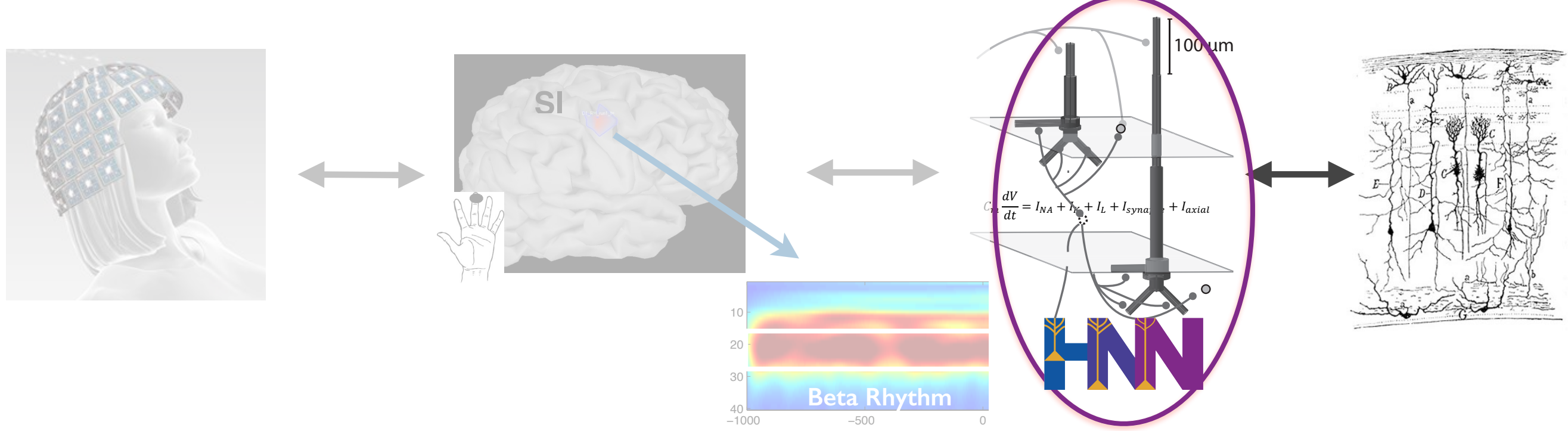


Aneth. Mouse CSD During Beta Event



Awake Monkey CSD During Beta Event





Applying HNN to study mechanisms by which beta inhibits perception

What does beta look like in *unaveraged* data?

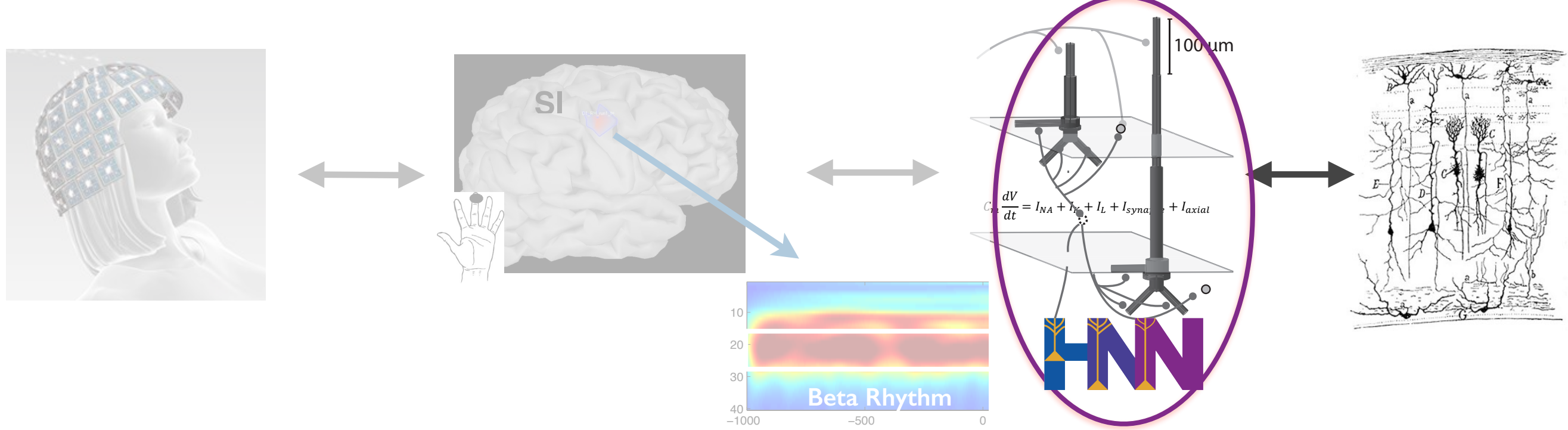
Beta “events” are transient (<150ms) with a stereotypical waveform.

What features underly functionally relevant differences in average power?

The number of beta events is greater during non-detected / non-attended trials, and non-detected trials have more recent beta events.

What are the circuit mechanisms underlying these differences?

Beta events emerge from a broad proximal excitatory synaptic drive simultaneous with a strong distal drive that last one beta period ~50ms.



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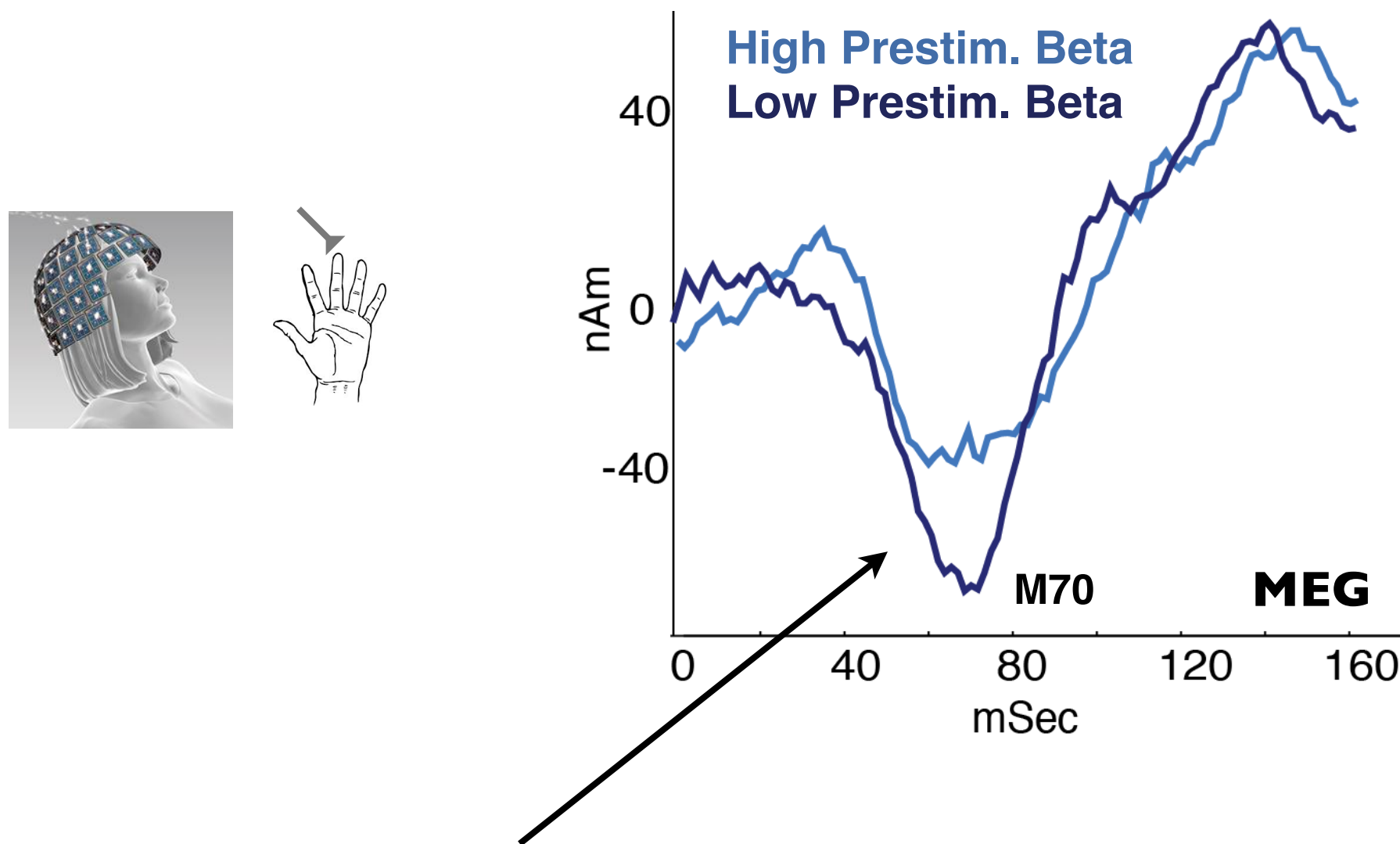
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How do these mechanisms translate to inhibited perception?

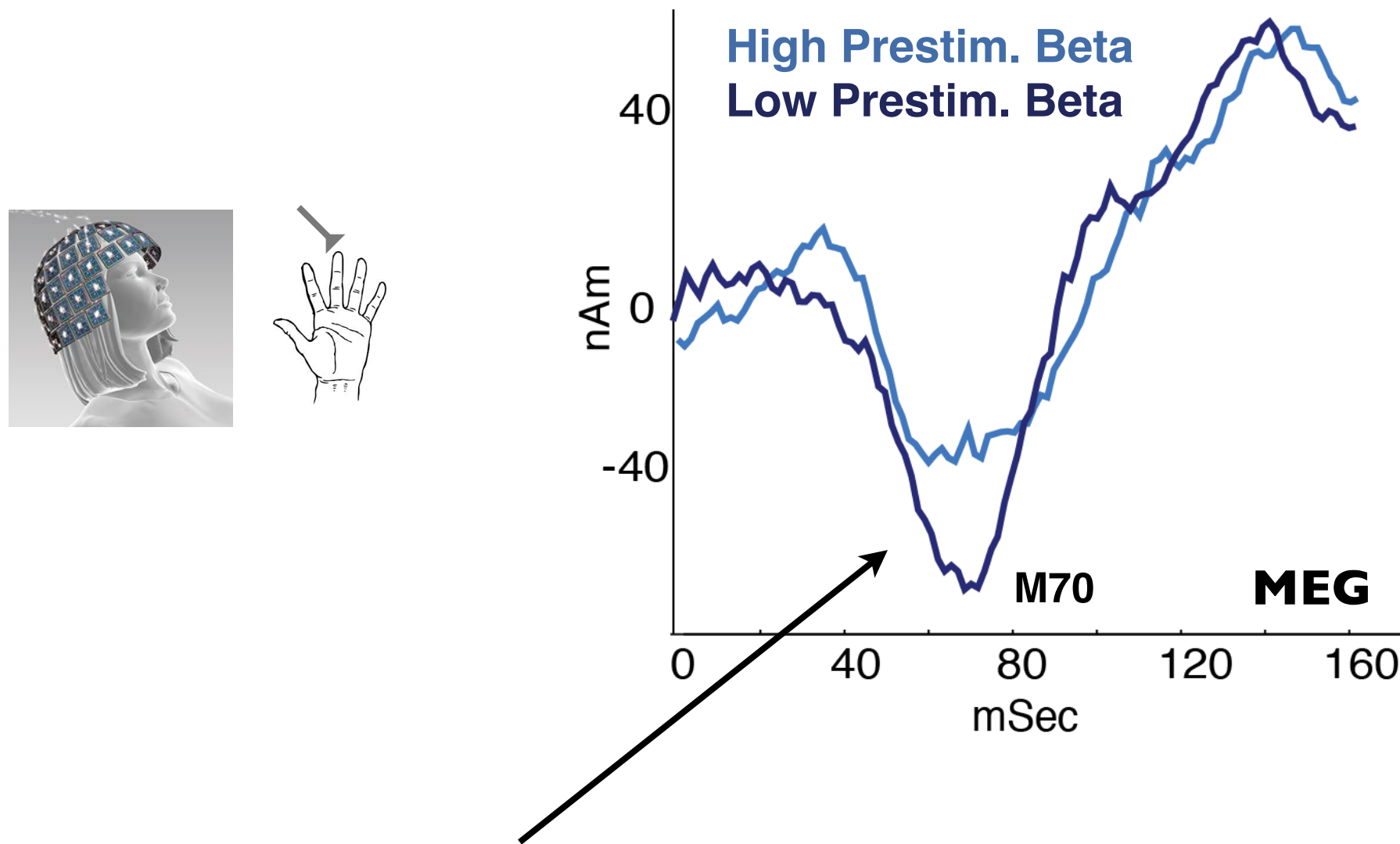
Beta Decreases Tactile Evoked Response Peaks that Predict Detection



Beta decreases M70 peak.

Smaller M70 implies less likely to detect stimulus. (*Jones et al. J. Neurosci. 2007*)

Beta Decreases Tactile Evoked Response Peaks that Predict Detection

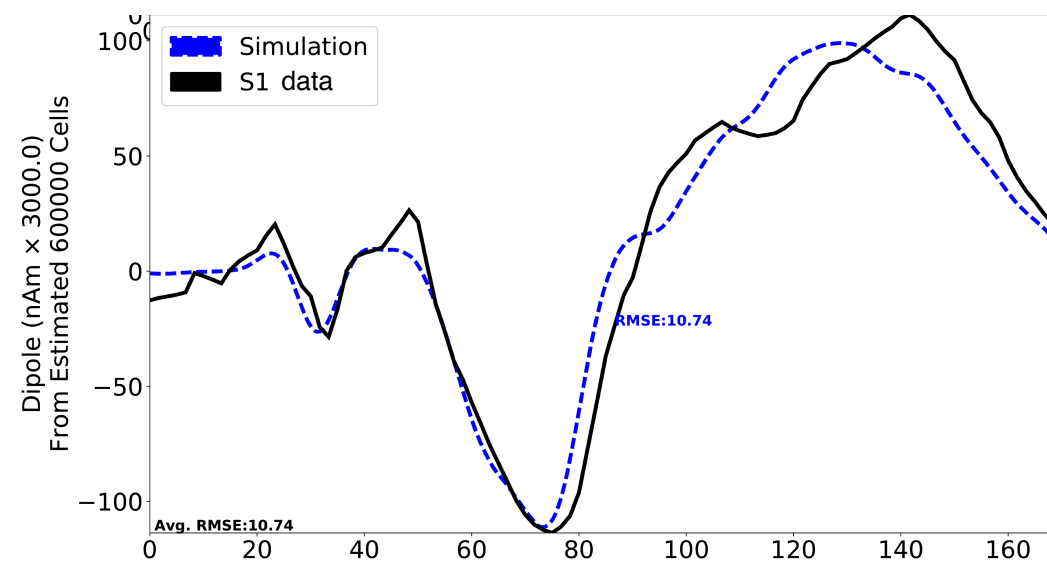
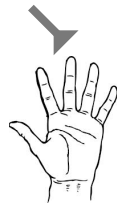


Beta decreases M70 peak.

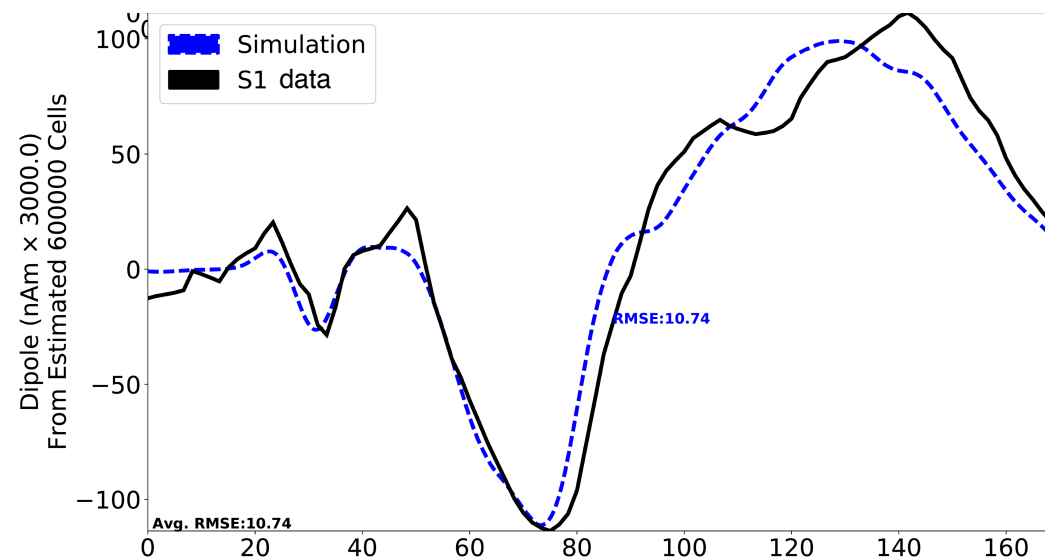
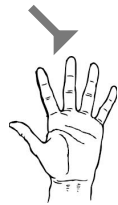
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Why?

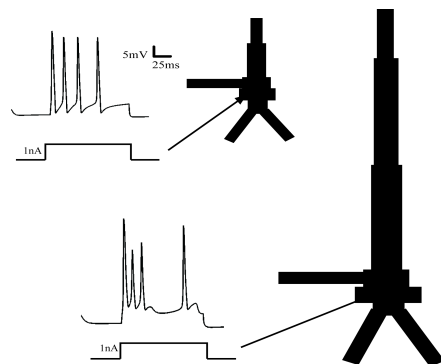
Human Neocortical Neurosolver Shows Layer Specific Sequence of Drive Generates ERP



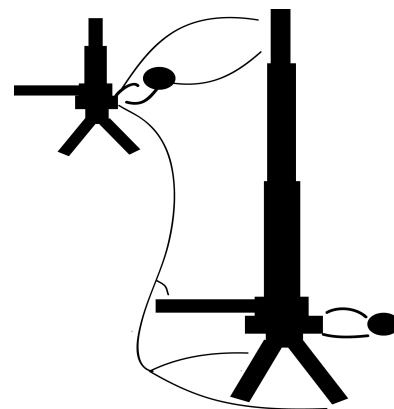
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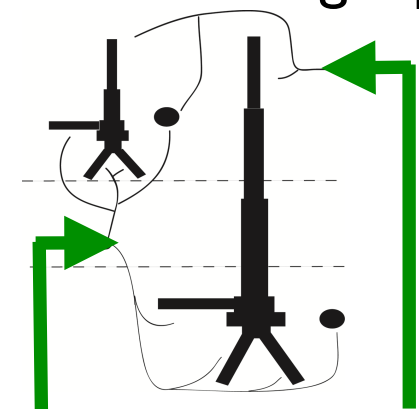
Fix Cellular Physiology



Fix Network Connectivity



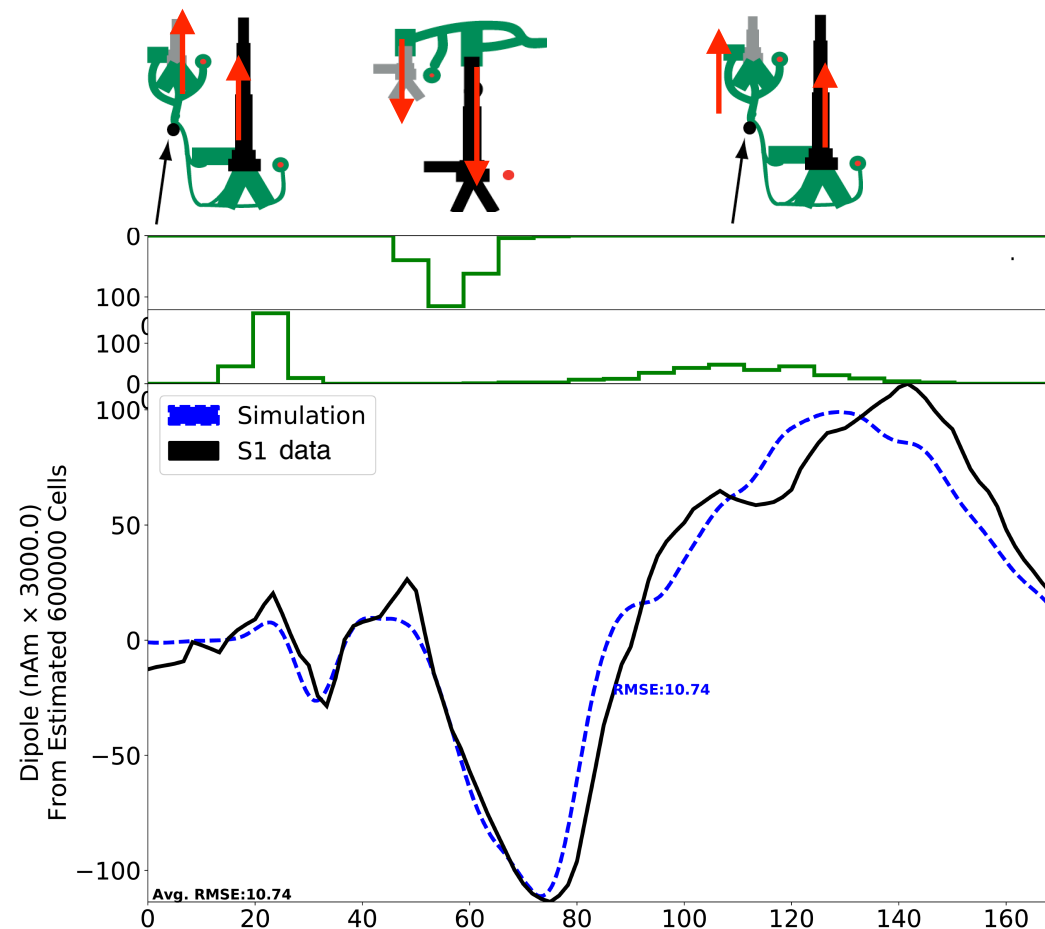
Adjust Strength & Timing of the Driving Inputs



Proximal Drive

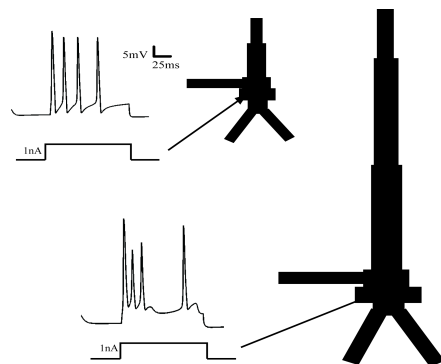
Distal Drive

Human Neocortical Neurosolver Shows Layer Specific Sequence of Drive Generates ERP

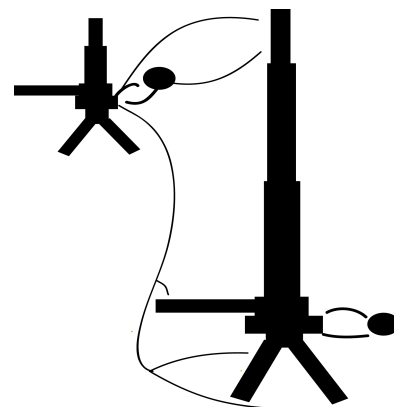


Supported by invasive recordings;
Cauler & Kulics 1991
Schroeder et al. 1995
Ikeda, Wang, Okada 2005
Lipton & Schroeder 2006

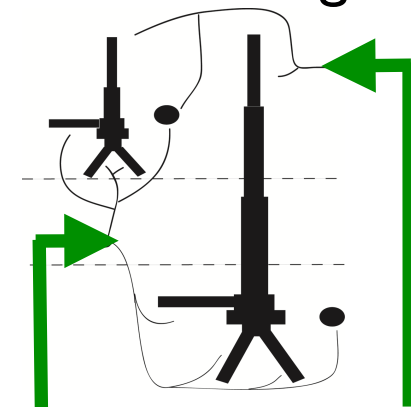
Fix Cellular Physiology



Fix Network Connectivity



Adjust Strength & Timing of the Driving Inputs



||||| ...

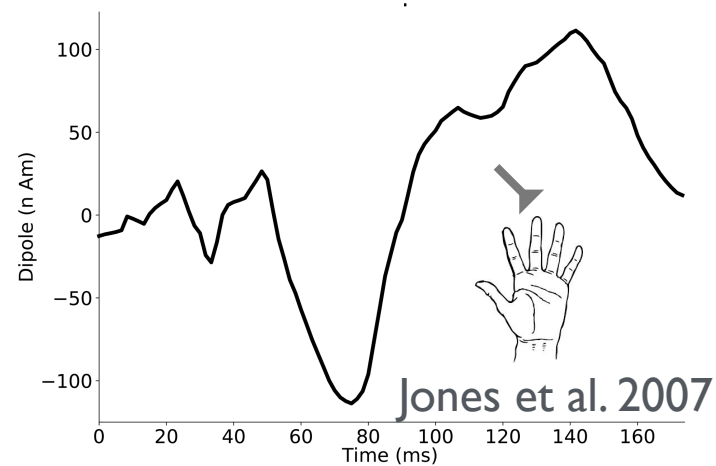
Proximal Drive

||||| ...

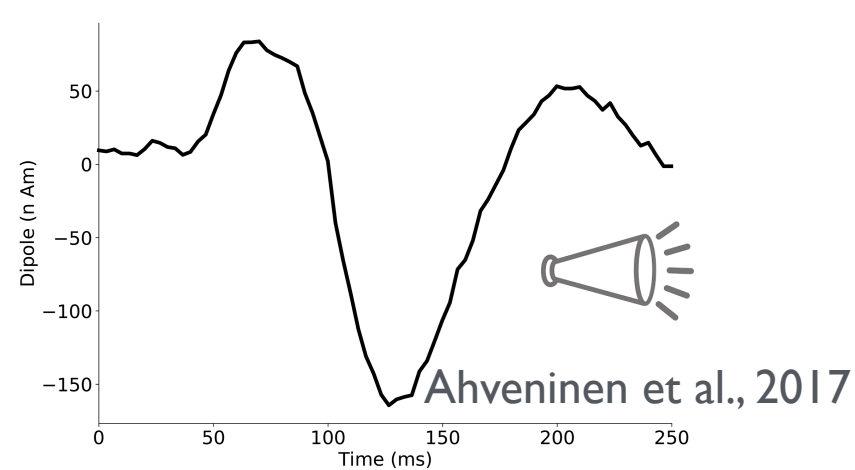
Distal Drive

Human Neocortical Neurosolver Shows Common Sequence of Drive Can Generate ER Similarities

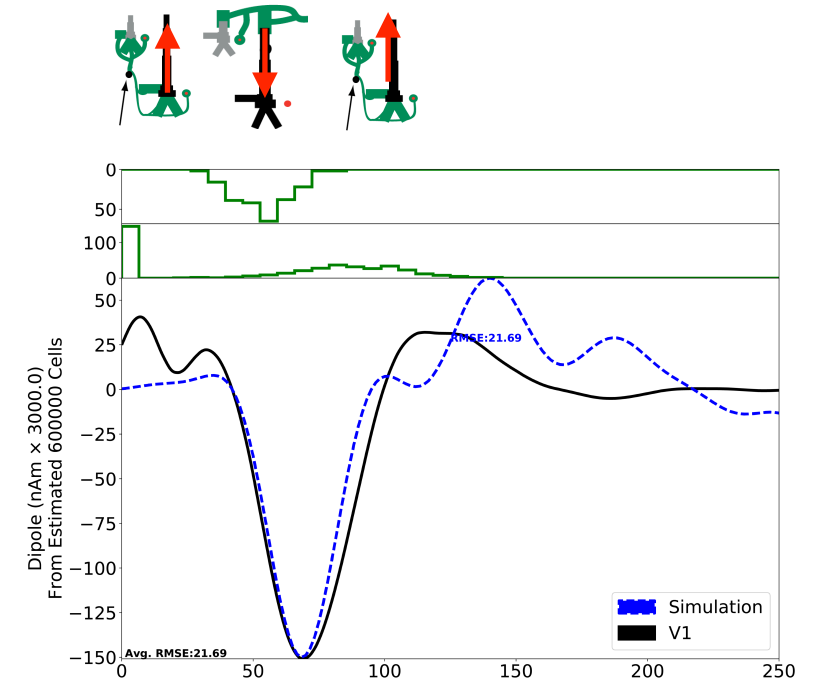
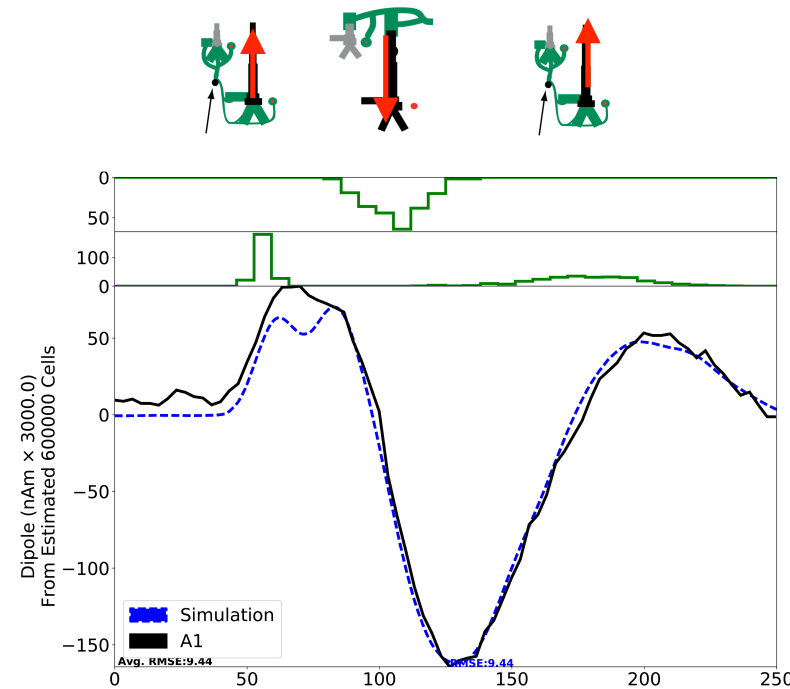
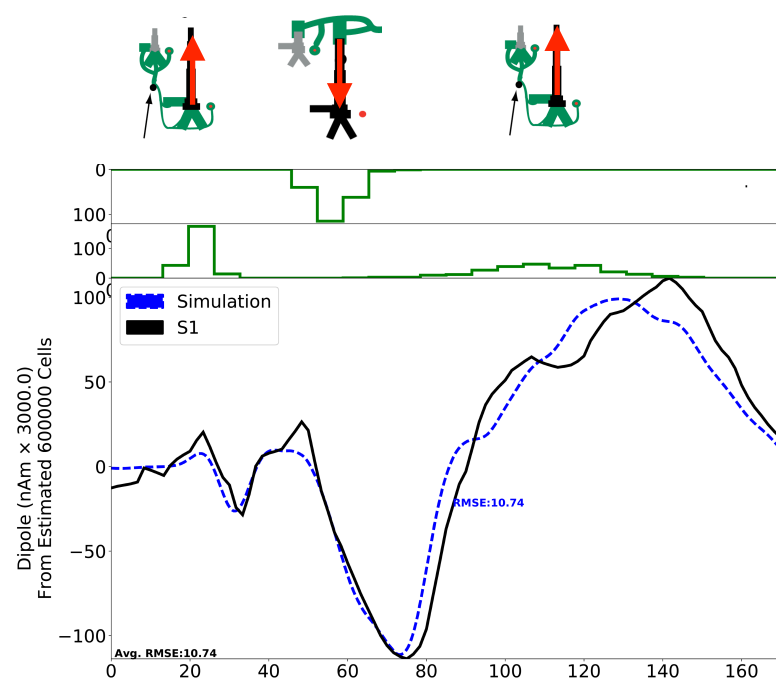
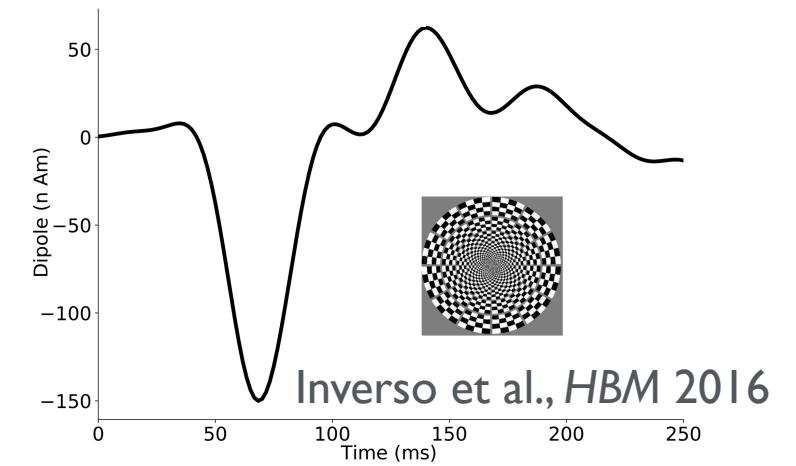
SI



A1



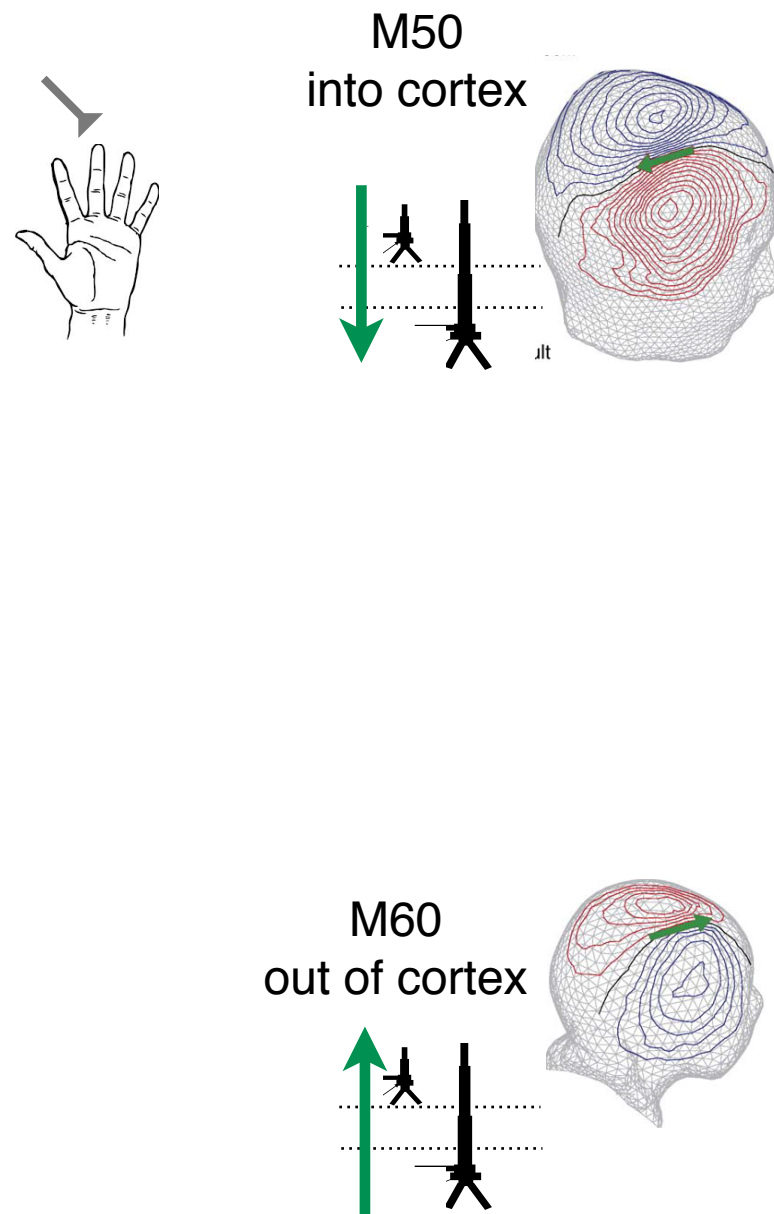
V1



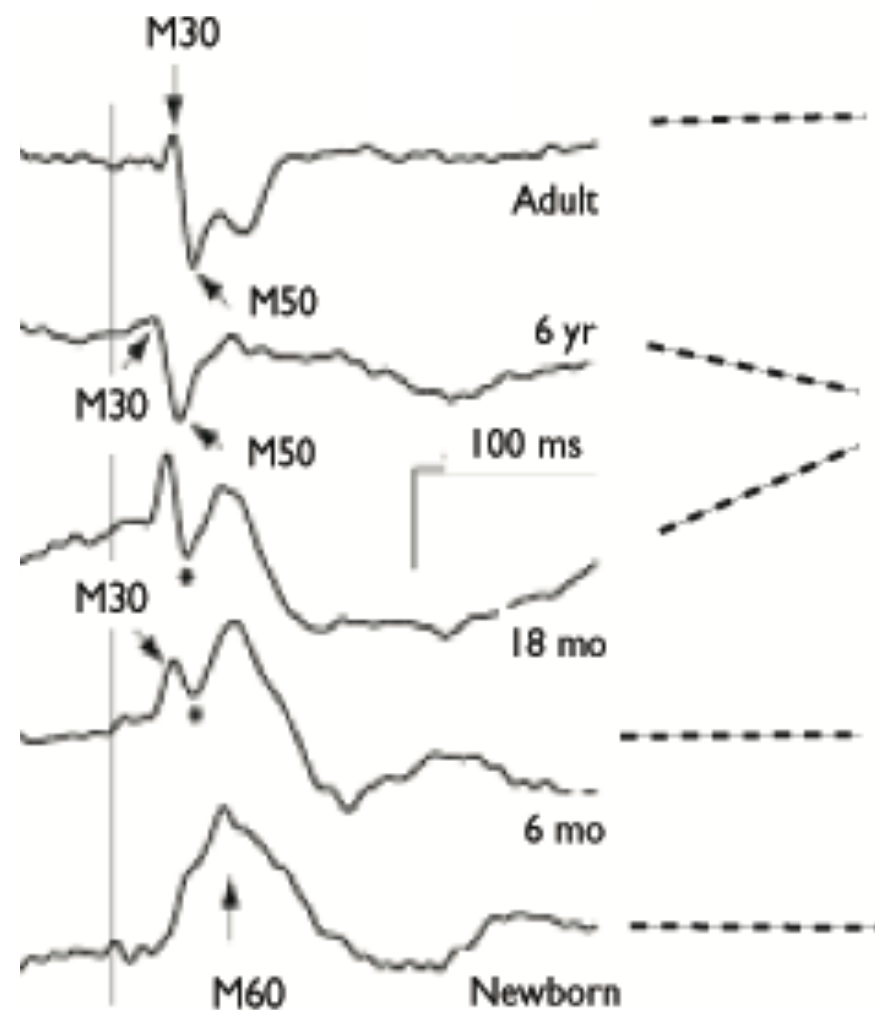
unpublished results

* tuned timing and strength of the exogenous proximal and distal drive

Human Neocortical Neurosolver Shows Development Changes in SEFs Can Emerge From Increased Distal Drive

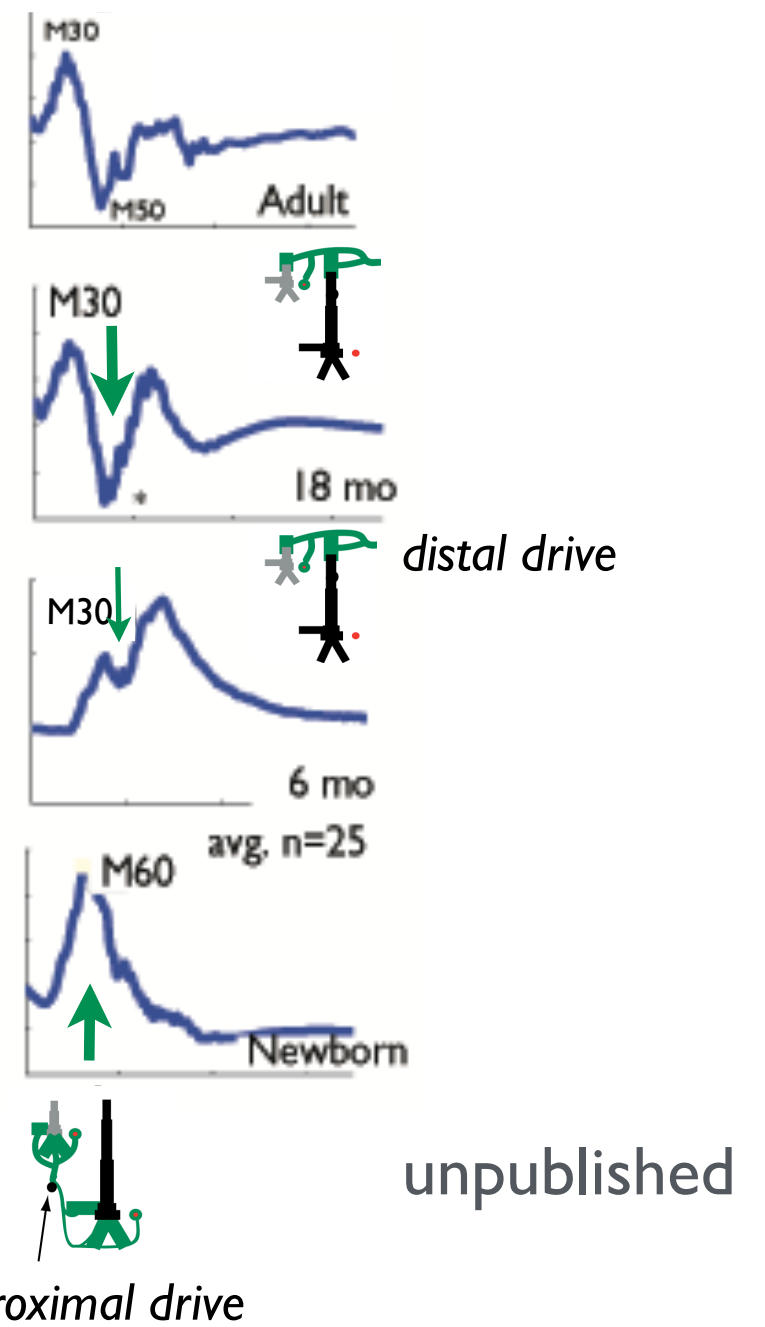


MEG



Lauronen... Pihko *Neuroimage* 2006;
Pihko...Okada *Clinical Neurophys.* 2009

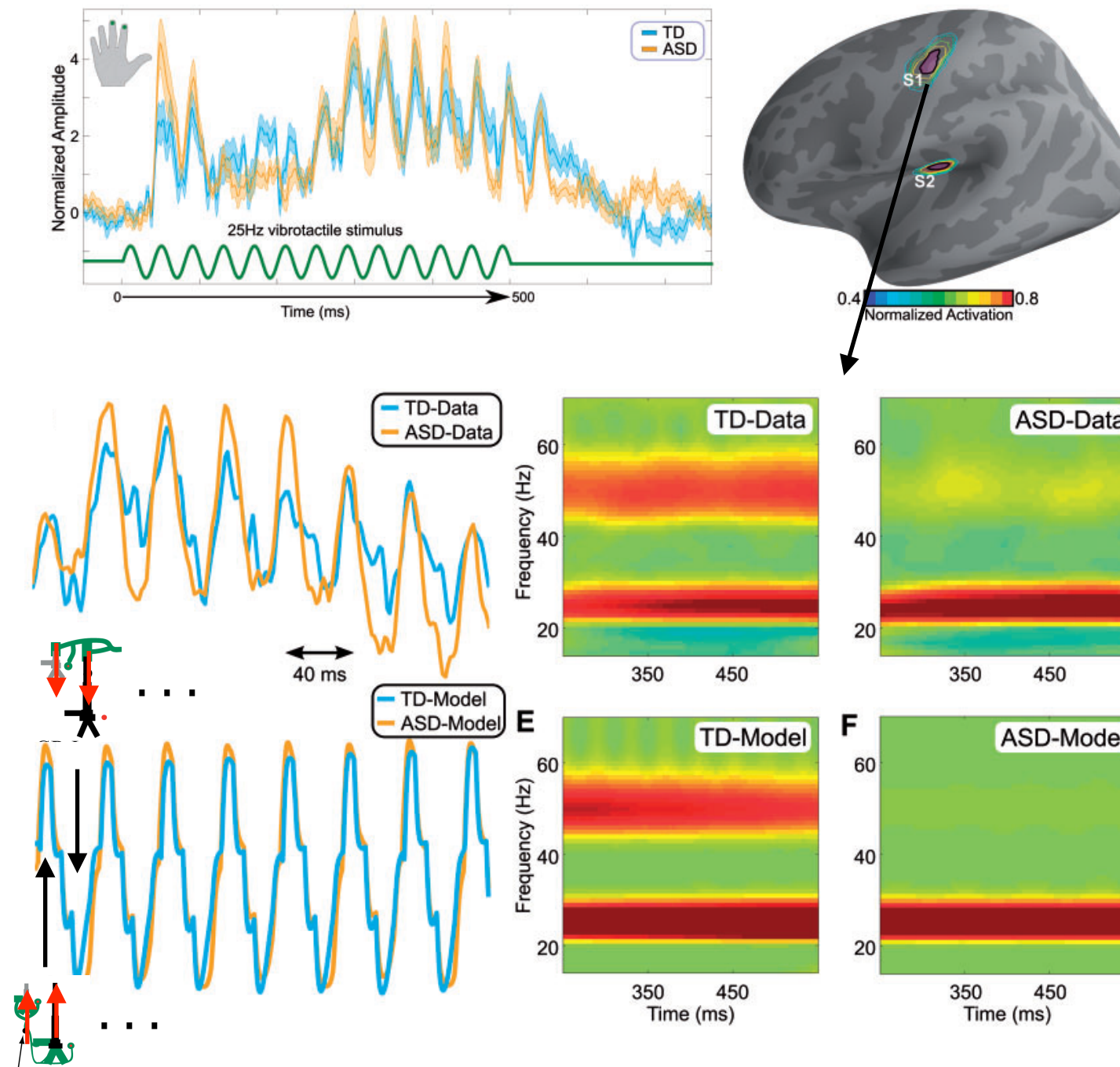
HNN Model



Both exogenous proximal and distal input (thalamus/higher order cortex)
and local network properties are critical to developmental changes

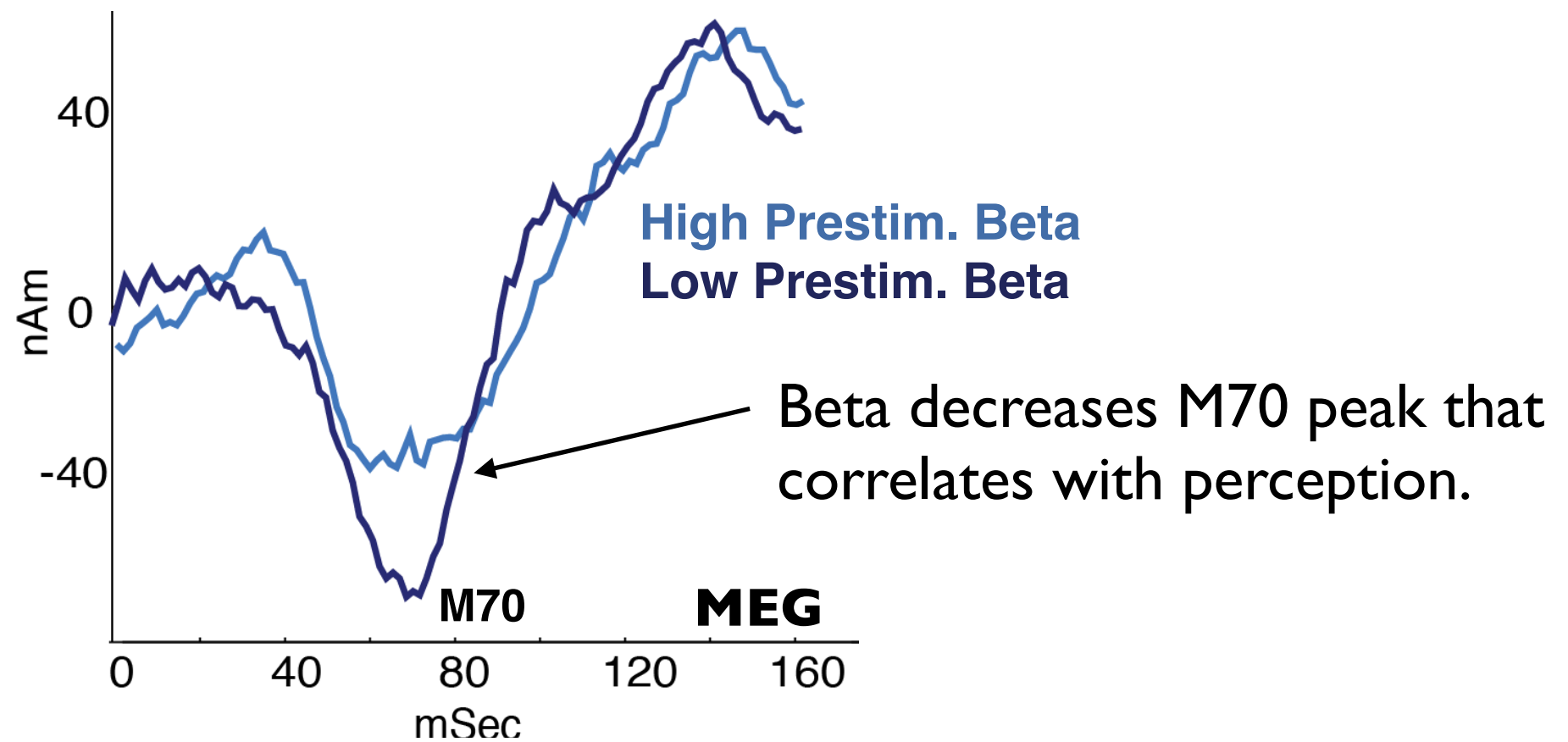
Human Neocortical Neurosolver Shows Differences in Steady State Tactile ERs in ASD can Emerge From Ratio of Feedforward & Feedback Connectivity

Khan... Kenet *BRAIN* 2015

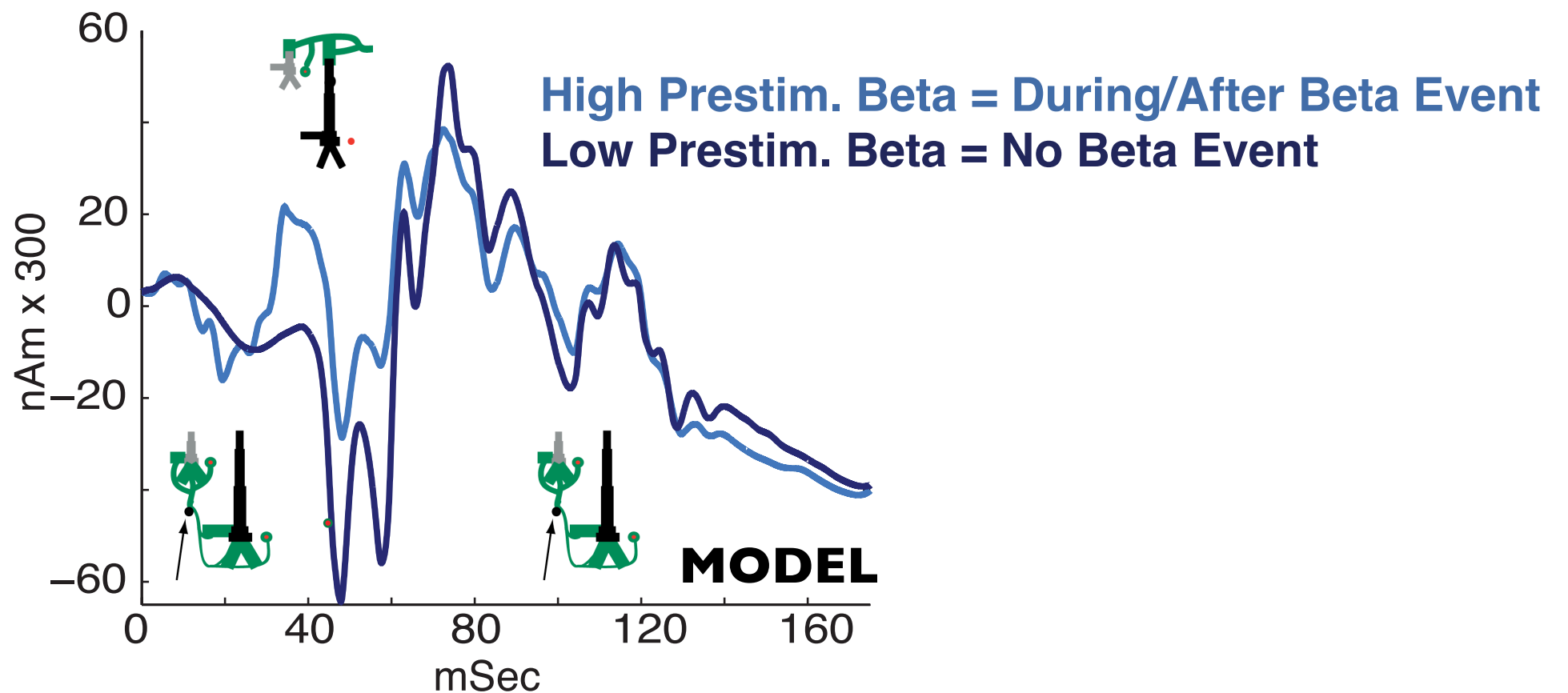
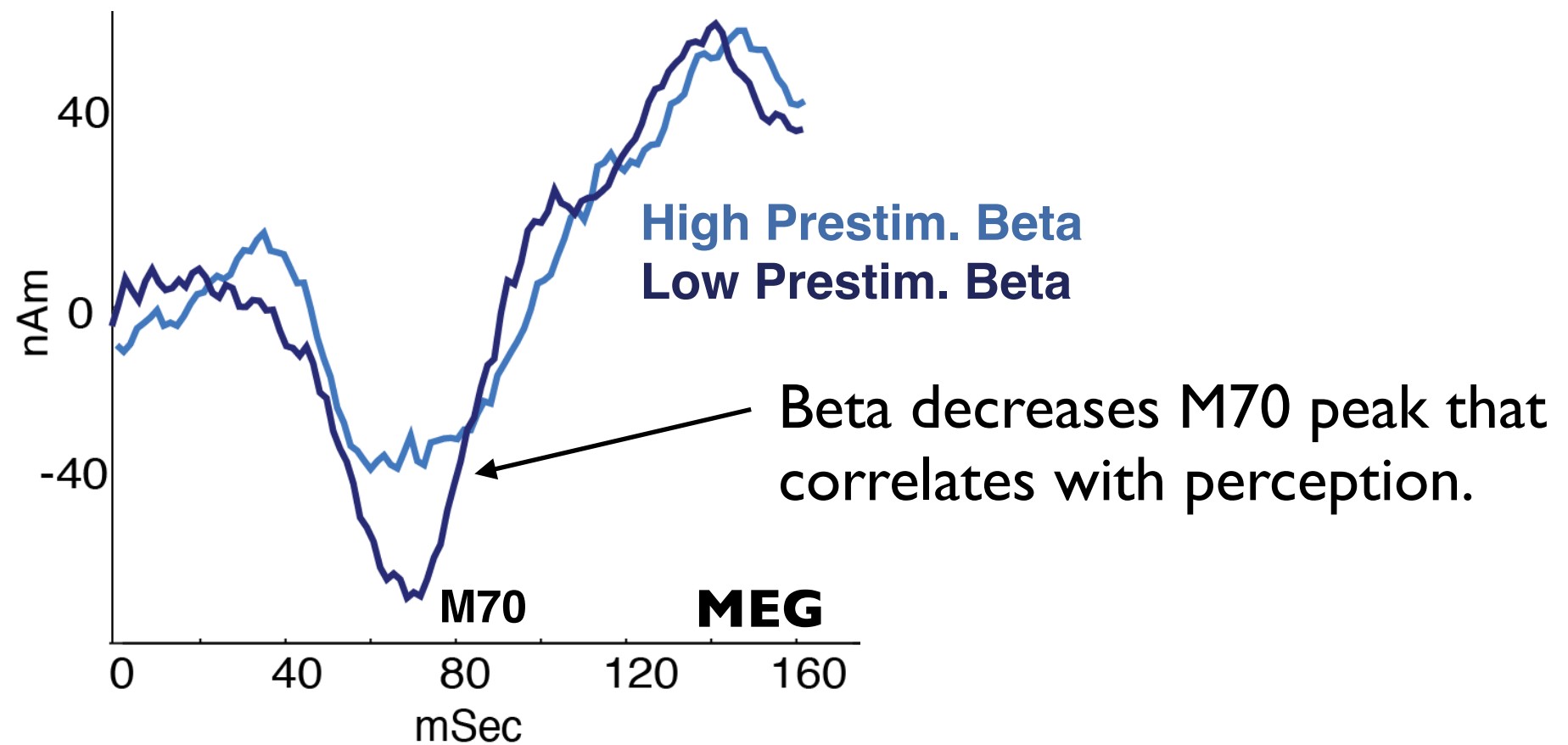


Data analysis suggested increased feedforward (S1-S2) and decreased feedback (S2-S1) connectivity. Increased feedforward relative to feedback drive in model reproduced correlates of ASD.

HNN Reproduces Beta's Impact on Tactile Evoked Response

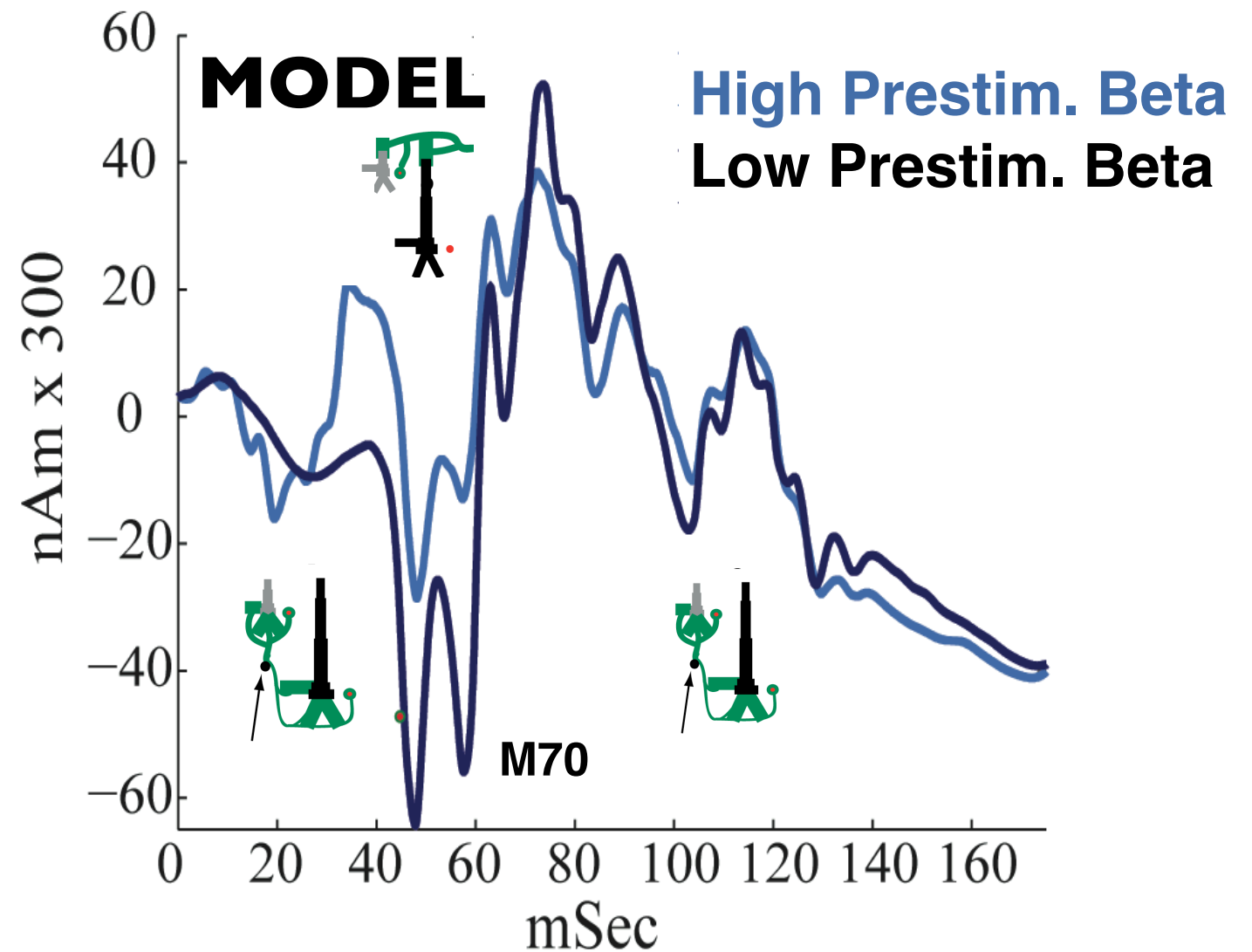
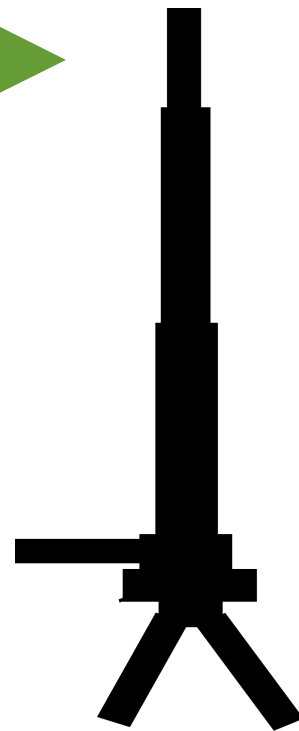


HNN Reproduces Beta's Impact on Tactile Evoked Response



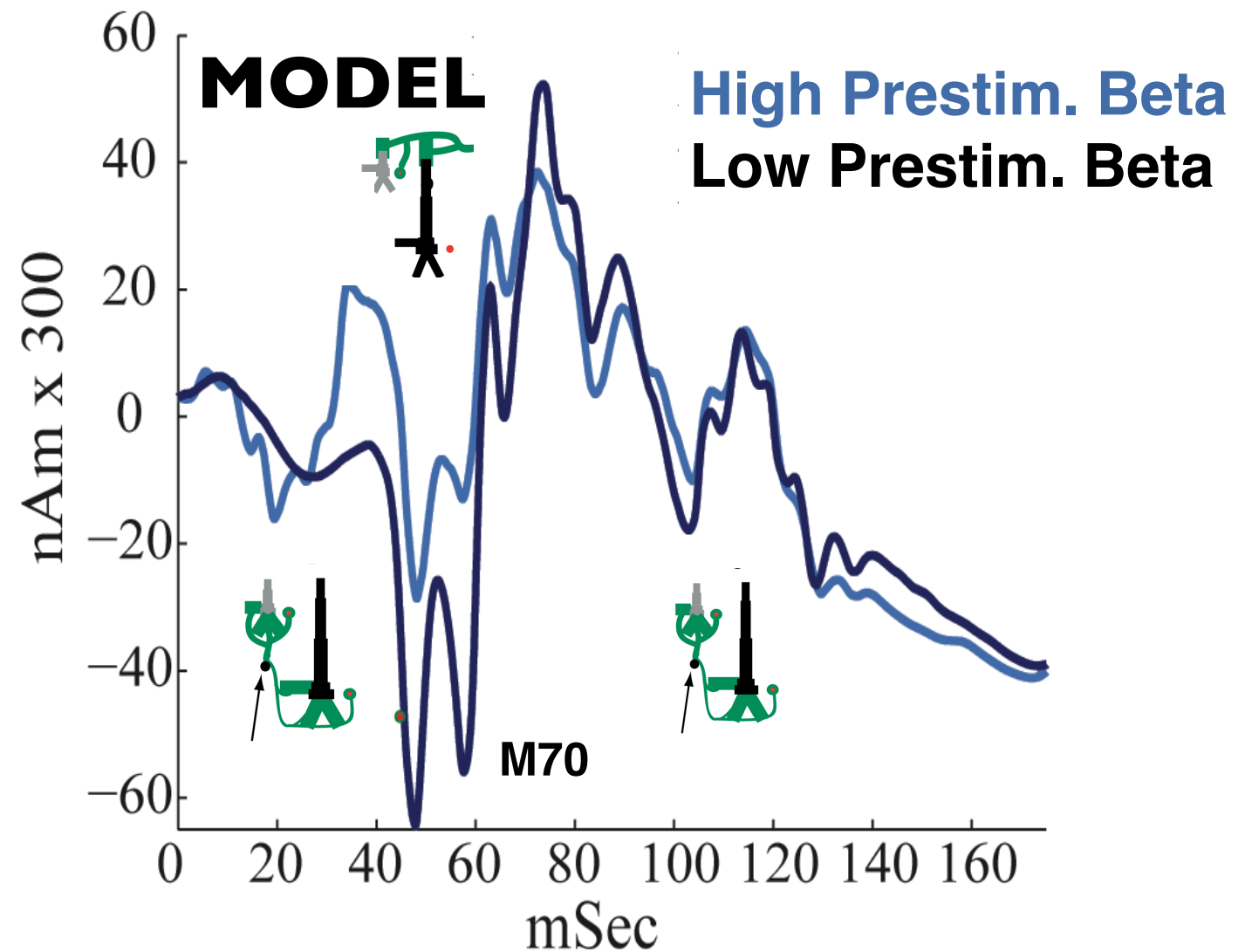
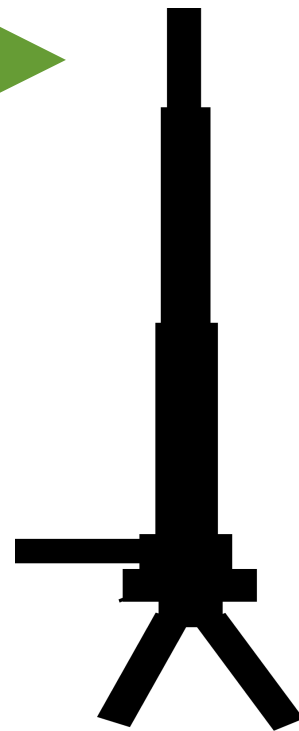
Beta Events Recruit Inhibition That Decreases the Downstream Relay of Sensory Information

Beta Created by Distal Drive



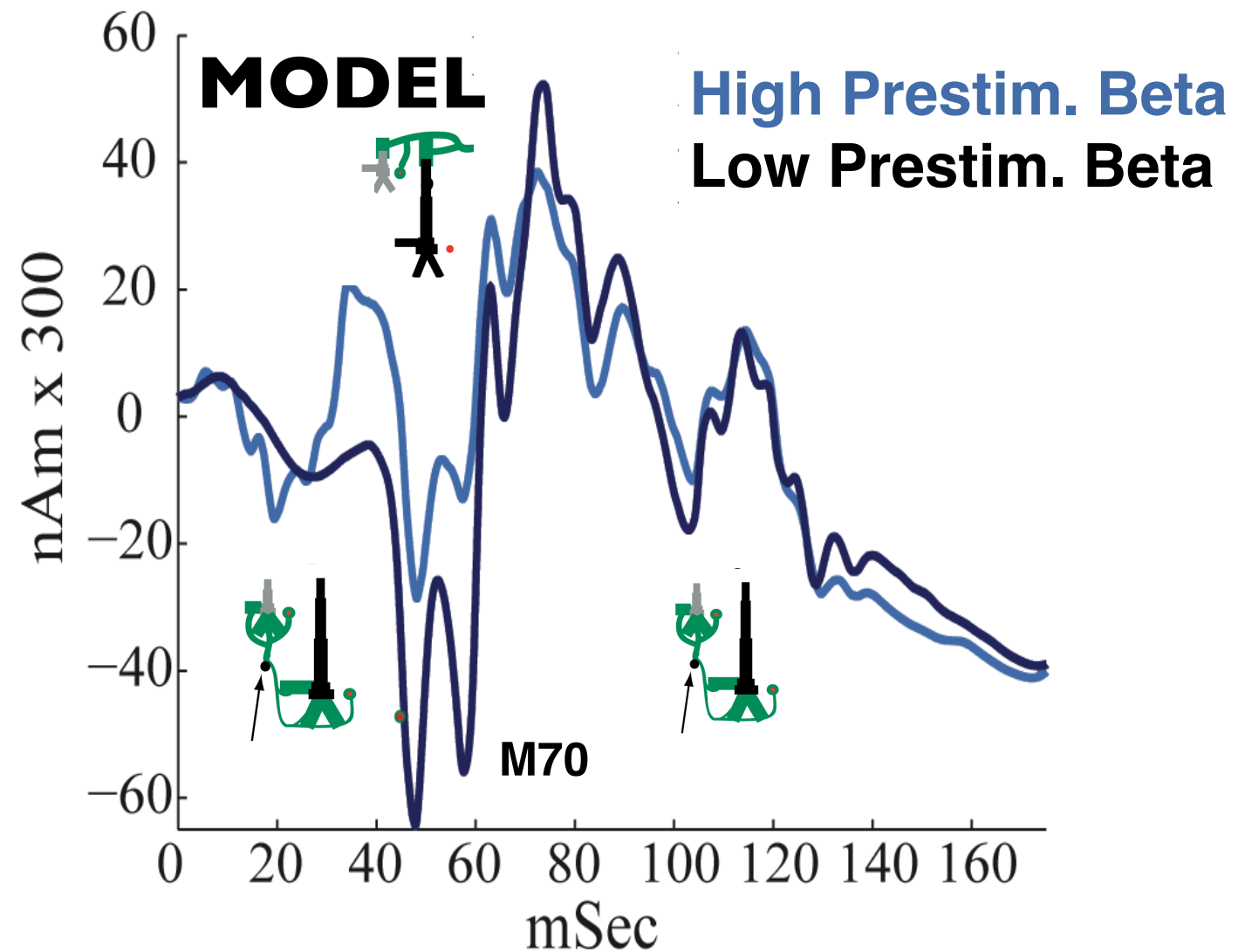
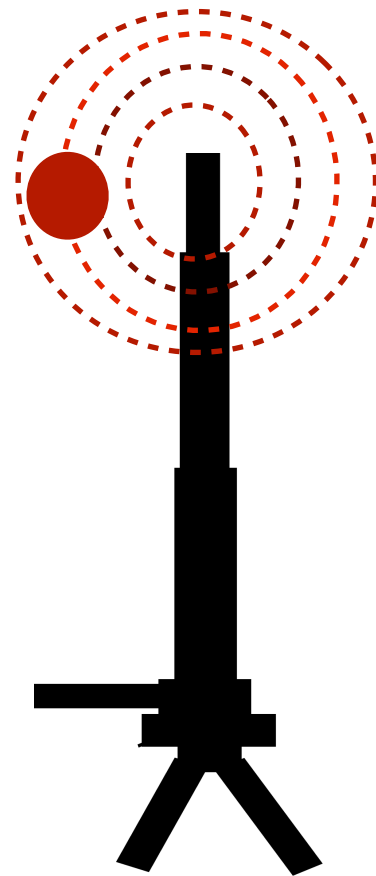
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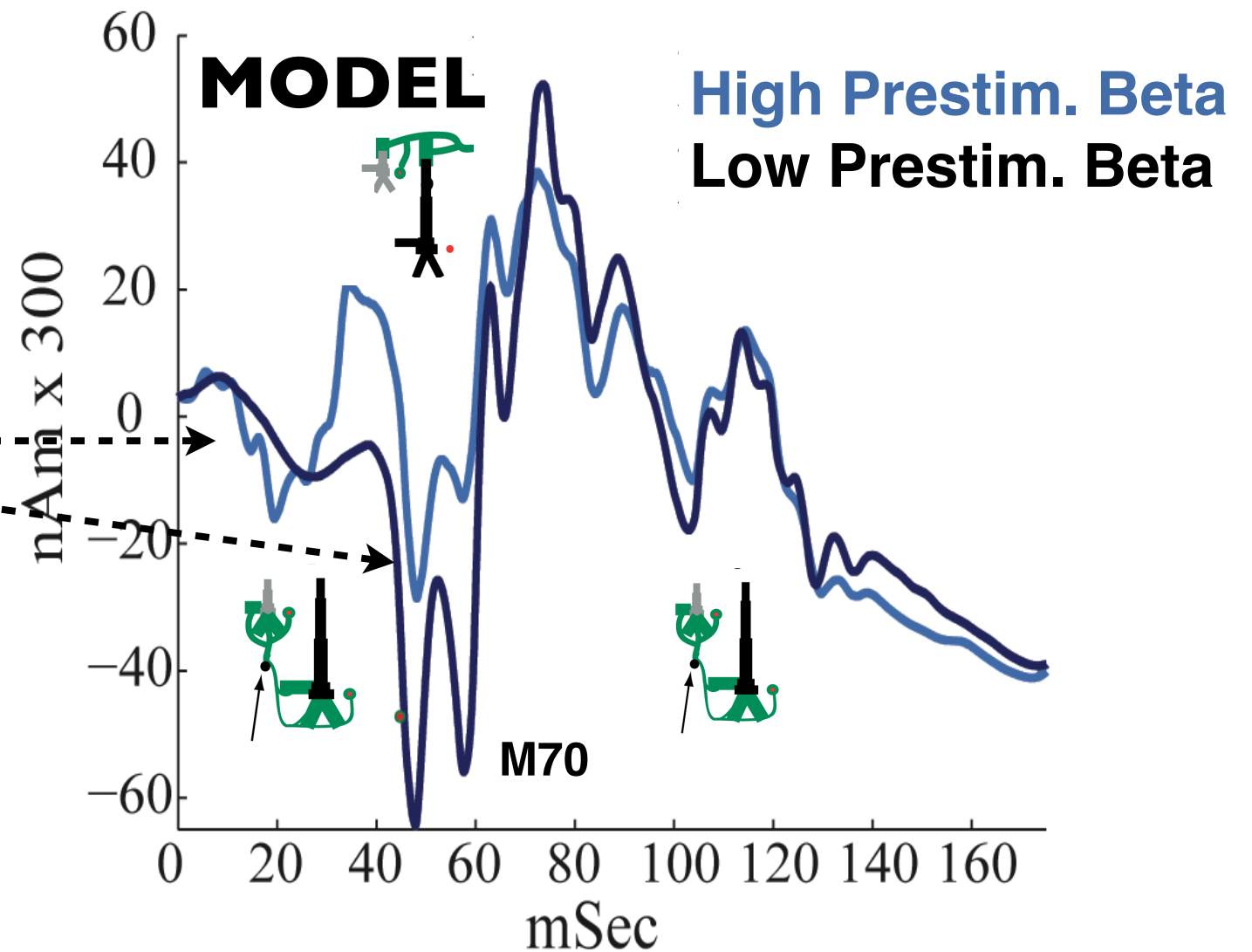
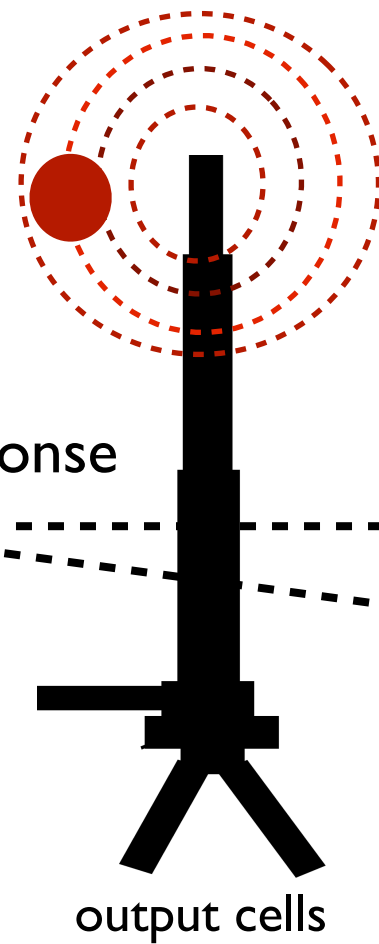
- High Beta Recruits More Supragranular Inhibition →



Beta Events Recruit Inhibition That Decreases the Downstream Relay of Sensory Information

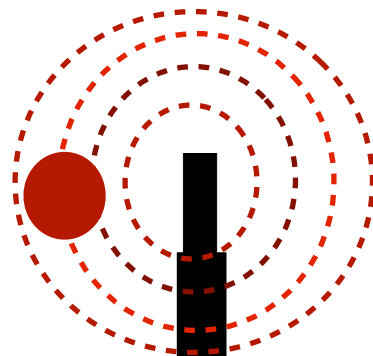
- High Beta Recruits More Supragranular Inhibition →

- Decreases Initial & M70 Response
- Overall Decrease Pyramidal Neuron Spiking



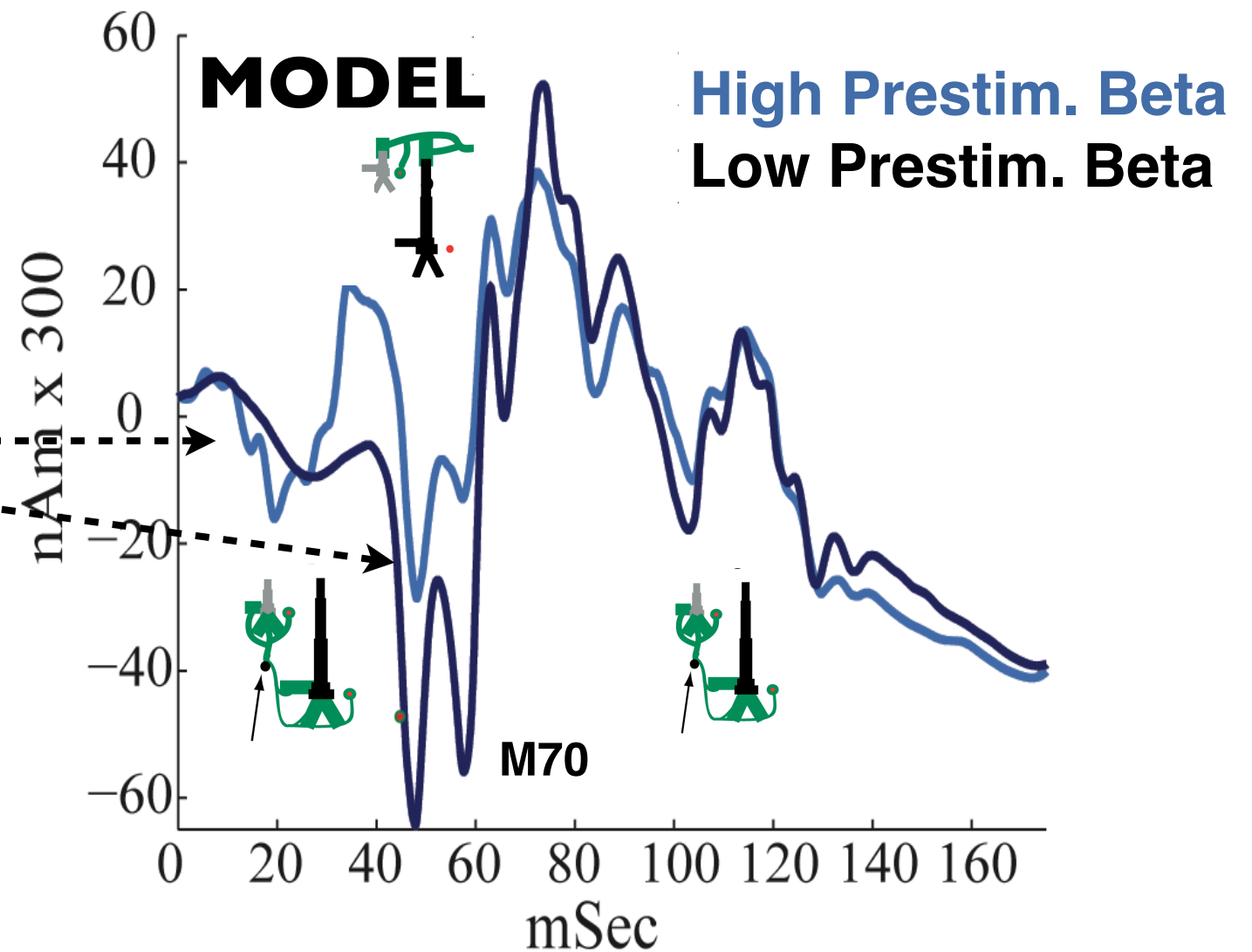
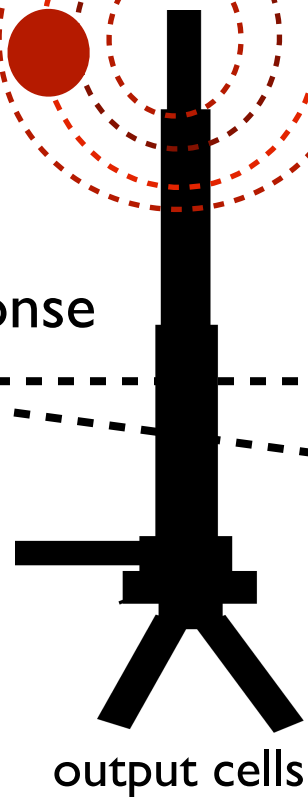
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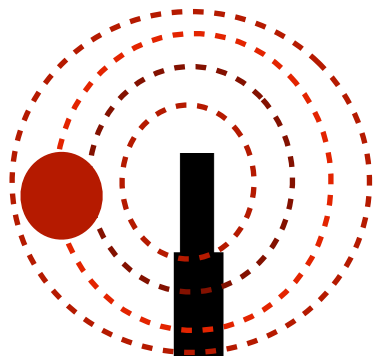
- Decreases Initial & M70 Response
- Overall Decrease Pyramidal Neuron Spiking

- Decreases Downstream Relay of Early Information Out of SI



Beta Events Recruit Inhibition That Decreases the Downstream Relay of Sensory Information

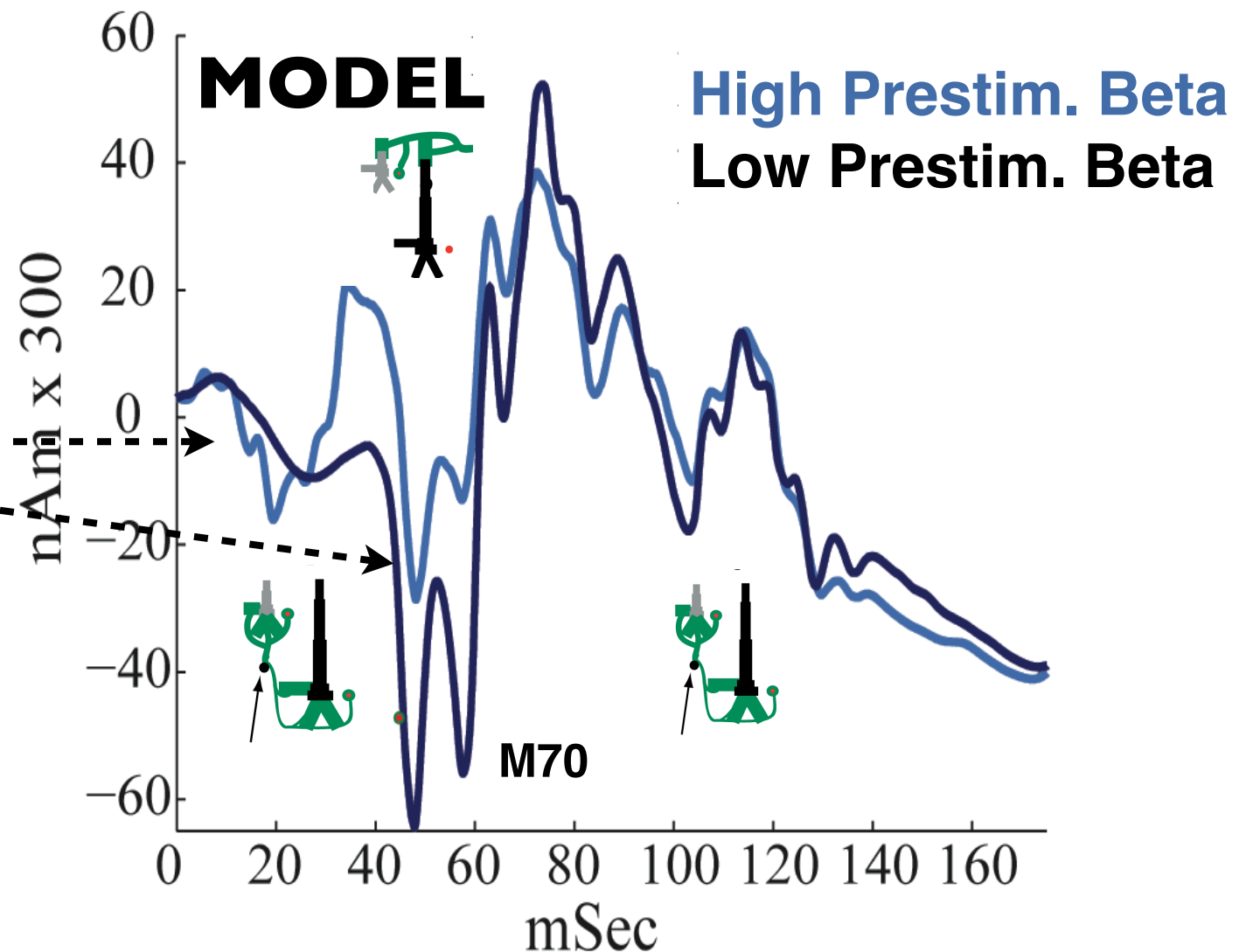
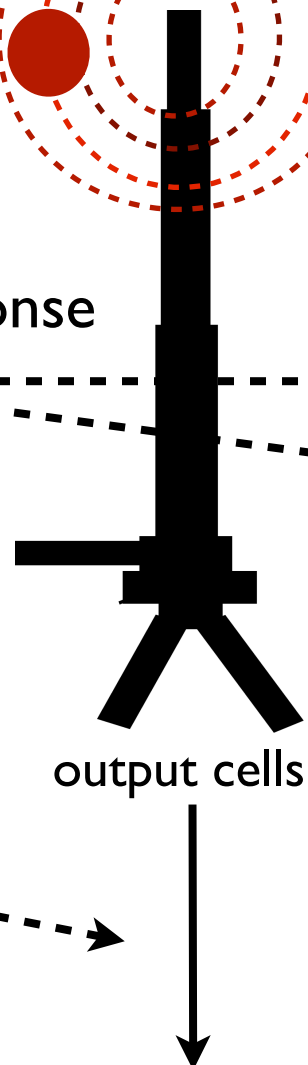
- High Beta Recruits More Supragranular Inhibition →

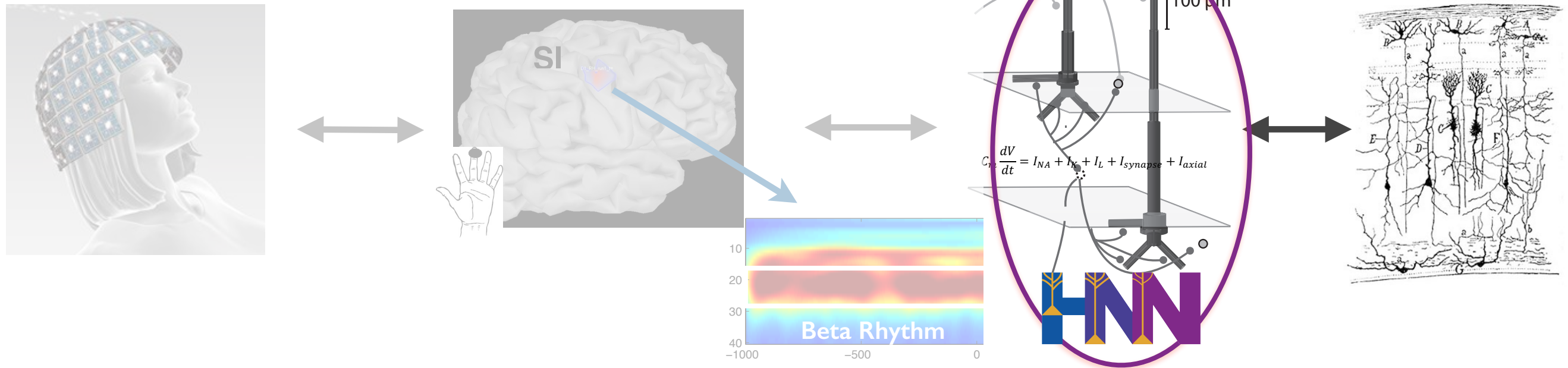


- Decreases Initial & M70 Response
- Overall Decrease Pyramidal Neuron Spiking

- Decreases Downstream Relay of Early Information Out of SI

- Decreases Probability of Perception





Applying HNN to study circuit mechanisms creating beta rhythms and to understand if and how they causally inhibit perception

What does beta look like in unaveraged data?

Beta “events” are transient (<150ms) with a stereotypical waveform.

What features underly functionally relevant differences in average power?

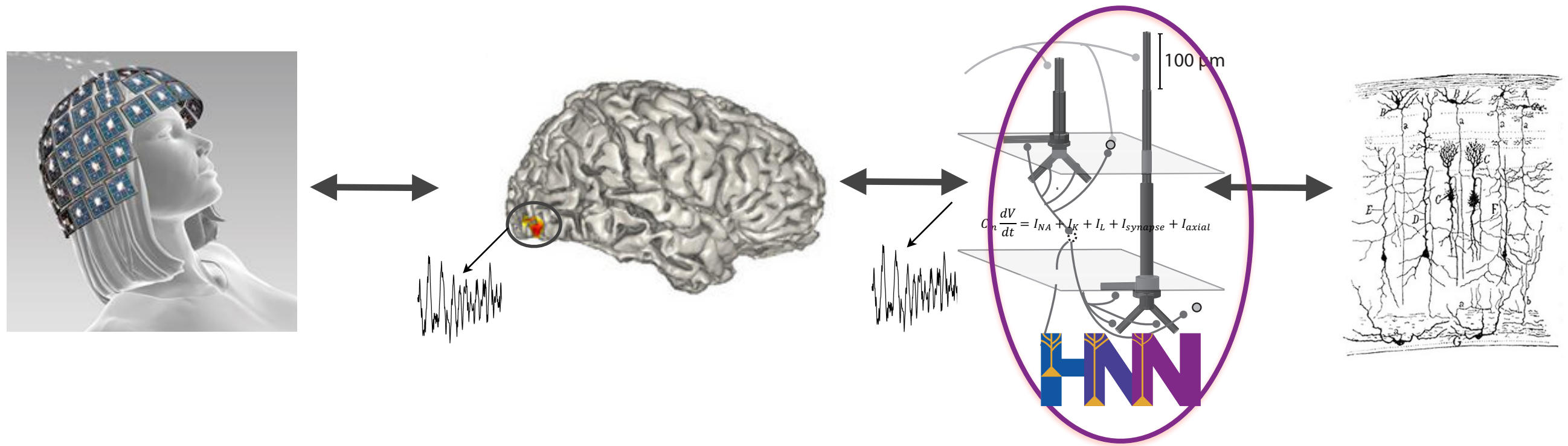
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What are the circuit mechanisms underlying these differences?

Beta events emerge from a broad proximal excitatory synaptic drive simultaneous with a strong distal drive that last one beta period ~50ms.

How do these mechanisms translate to inhibited perception?

Beta decreases the salience of sensory input via recruitment of supra-granular inhibition that decreases relay of sensory information.



Talk Outline

- Human Neocortical Neurosolver (HNN): A computational neural modeling tool for circuit level investigation of MEG/EEG signals generation
- HNN reveals novel mechanisms and meaning of brain rhythms and sensory evoked response
- A brief tour of HNN: GUI driven, open-source access, tutorials

[HOME](#)[UNDER THE HOOD](#)[TUTORIALS](#)[FEEDBACK](#)[DEVELOPMENT TEAM](#)[INSTALL](#)[FORUM](#)

Human Neocortical Neurosolver

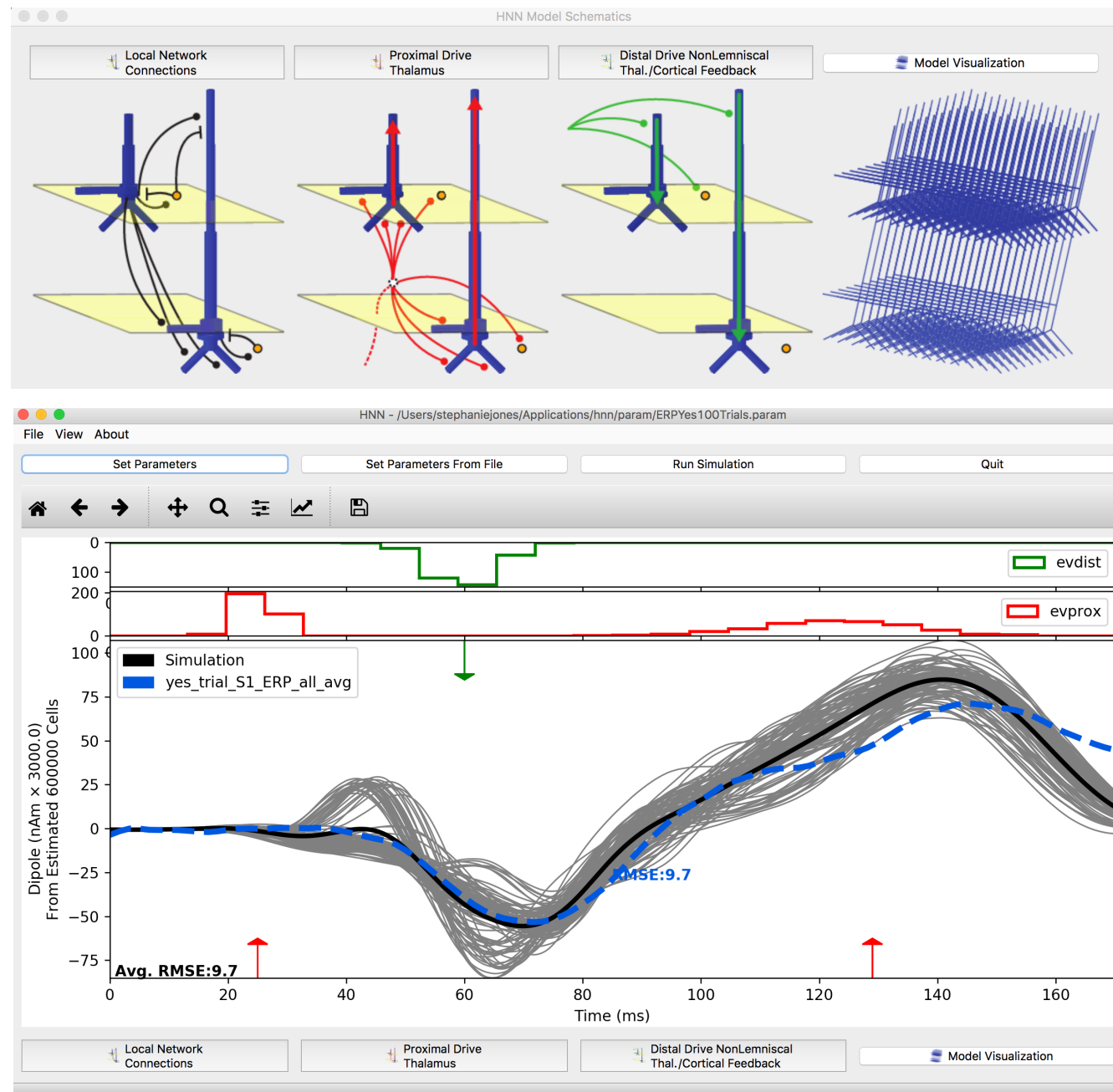
[SUBSCRIBE TO OUR GOOGLE GROUP](#)

Open Source Access : <https://hnn.brown.edu>

- Installation instructions (Linux, Windows, MAC)
- Tutorials on how to
 1. simulate sensory evoked responses
 2. simulate low frequency oscillations (alpha, beta, gamma)
 3. compare simulation to recorded data
 4. view layer specific dipoles & cell spiking and voltage activity
 5. perform time-frequency analysis
- “Under the Hood” Manual
- Users Forum

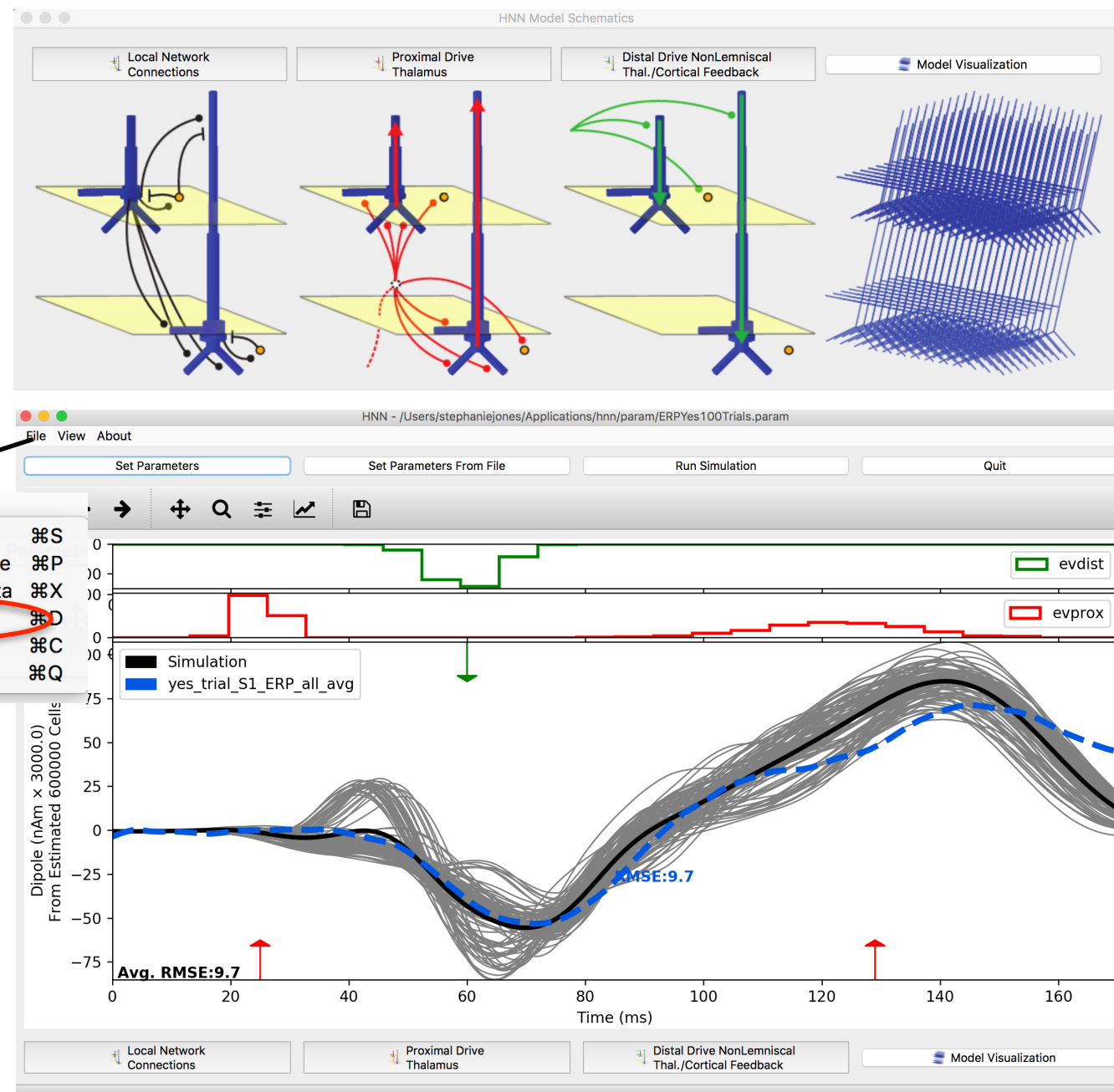
Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



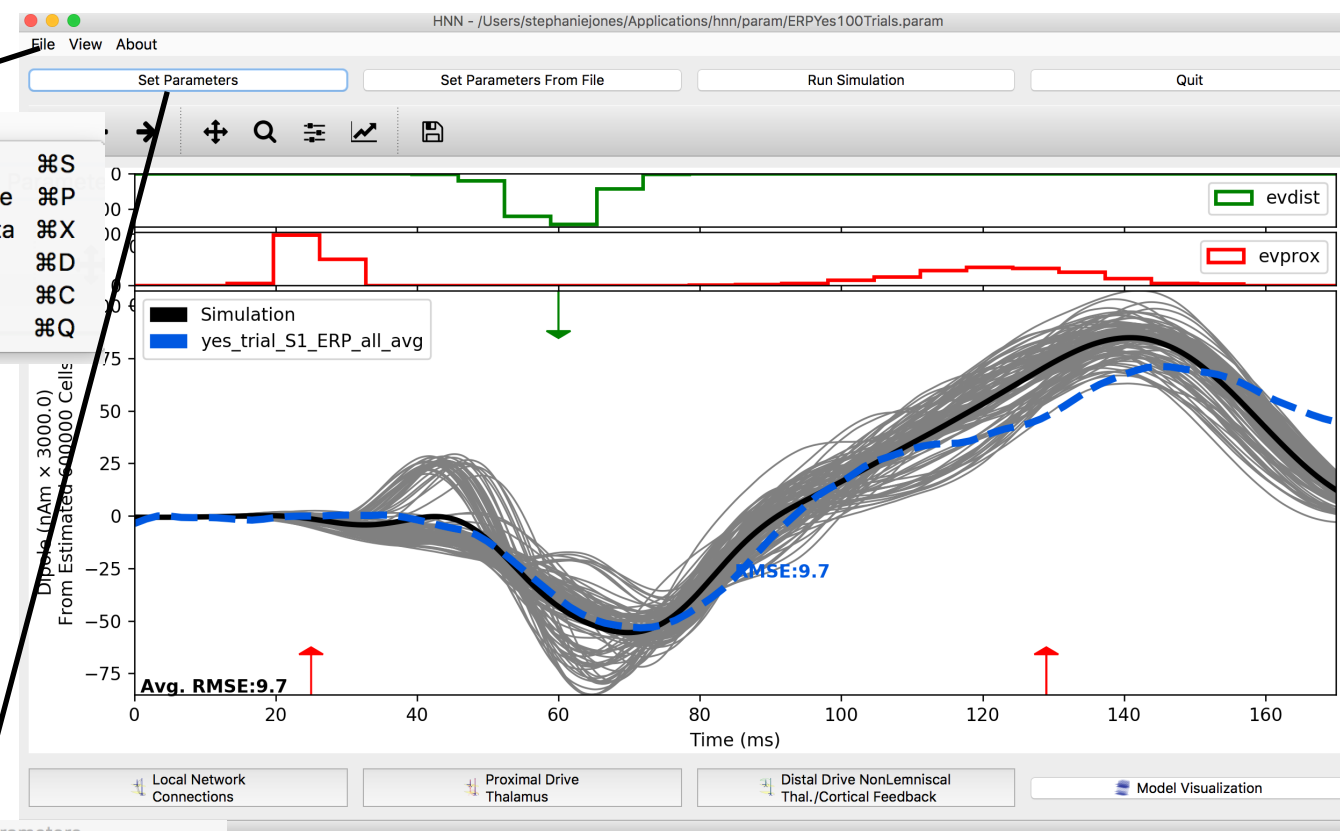
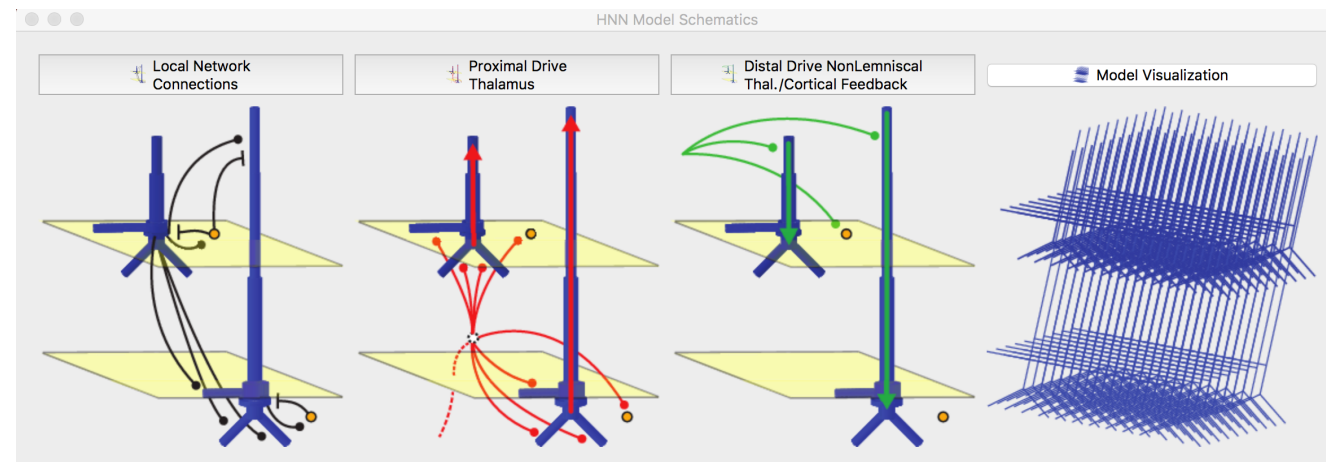
Human Neocortical Neurosolver

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Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



- File
- View
- About
- Run simulation ⌘S
- Set parameter file ⌘P
- Clear canvas/data ⌘X
- Load data file ⌘D
- Clear data file ⌘C
- Exit ⌘Q

Set Parameters

Simulation Name: default

Run Cell

Local Network Synaptic Gains

Rhythmic Proximal Inputs

Rhythmic Distal Inputs

Evoked Inputs

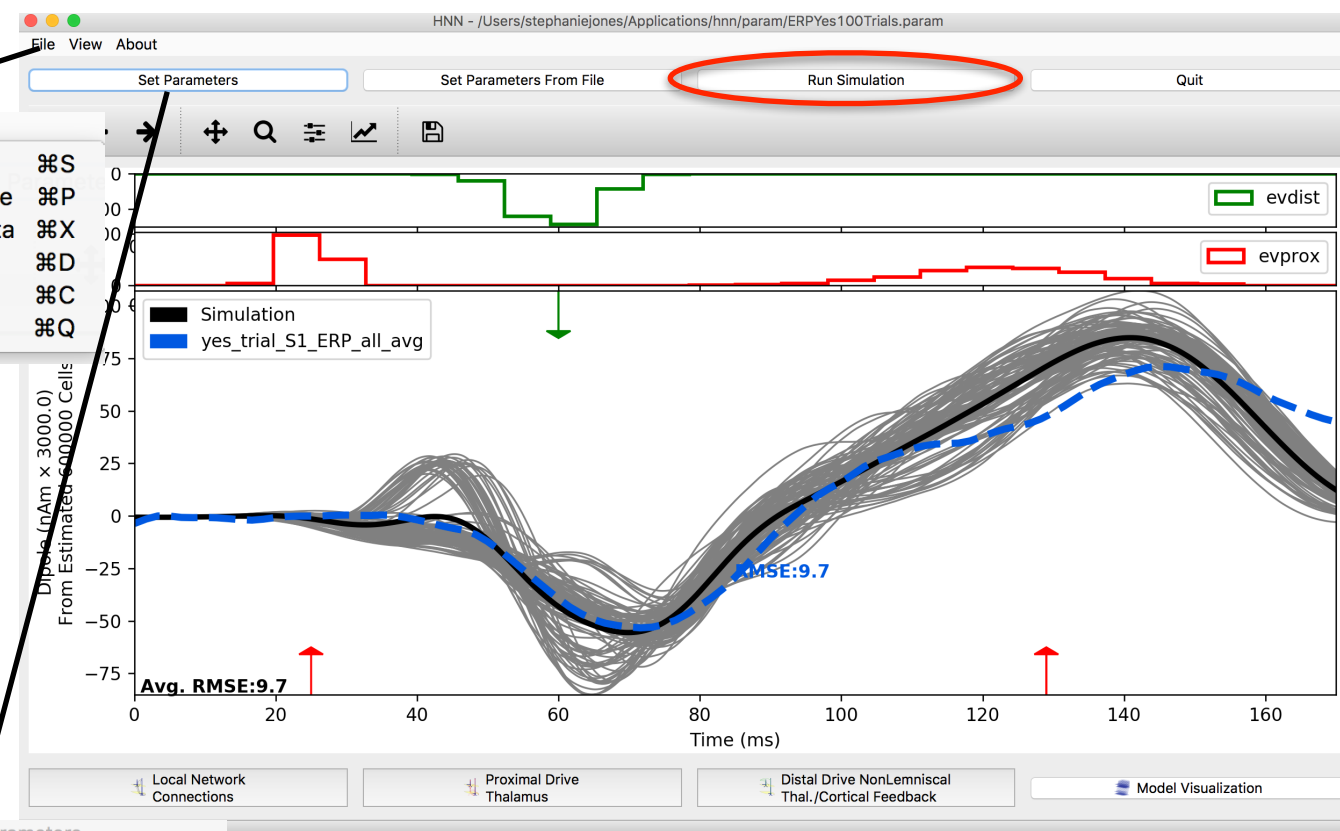
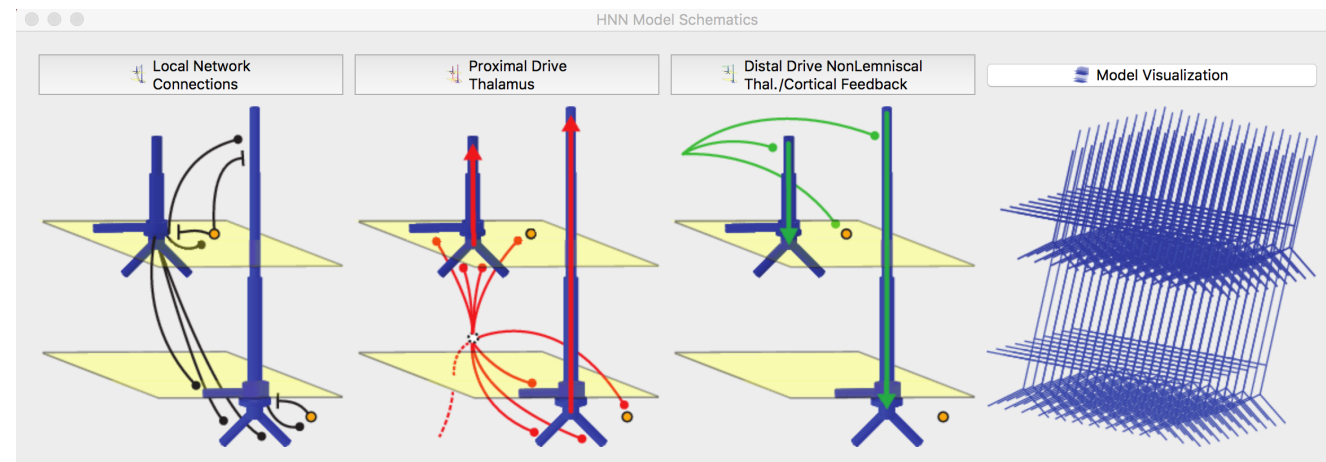
Poisson Inputs

Tonic Inputs

Save Parameters To File

Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



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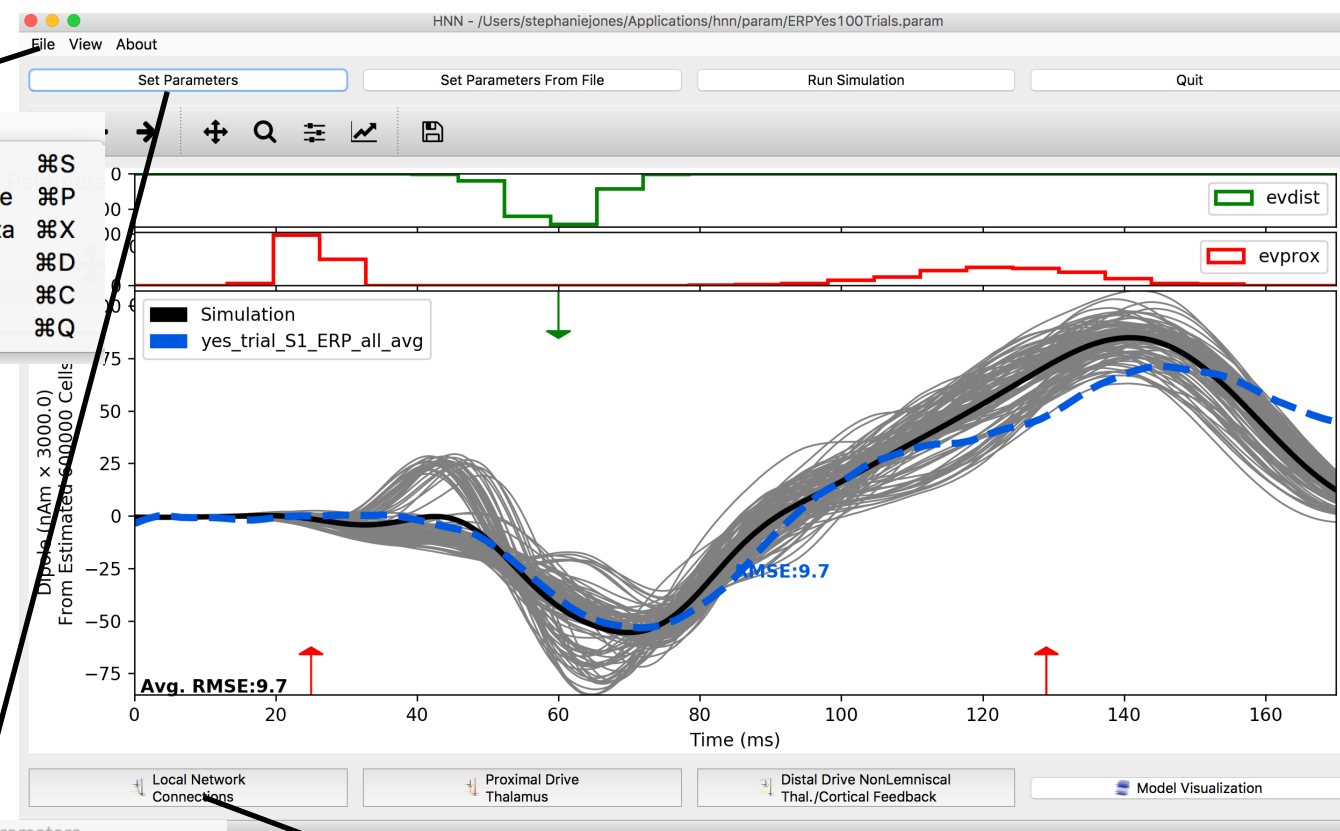
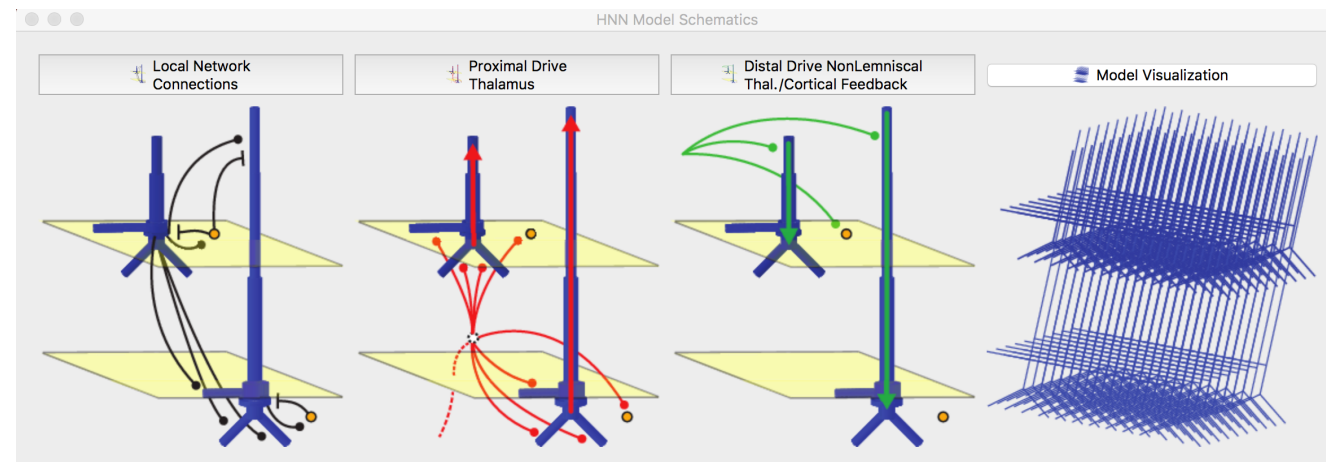
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- Load data file ⌘D
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- Exit ⌘Q

Set Parameters

Simulation Name: default

Run Cell

Local Network Synaptic Gains

Rhythmic Proximal Inputs

Rhythmic Distal Inputs

Evoked Inputs

Poisson Inputs

Tonic Inputs

Save Parameters To File

Local Network Parameters

Cells Layer 2/3 Pyr Layer 5 Pyr Layer 2/3 Bas Layer 5 Bas

L2/3 Pyr -> L2/3 Pyr AMPA weight (nS) 0.00110250000000

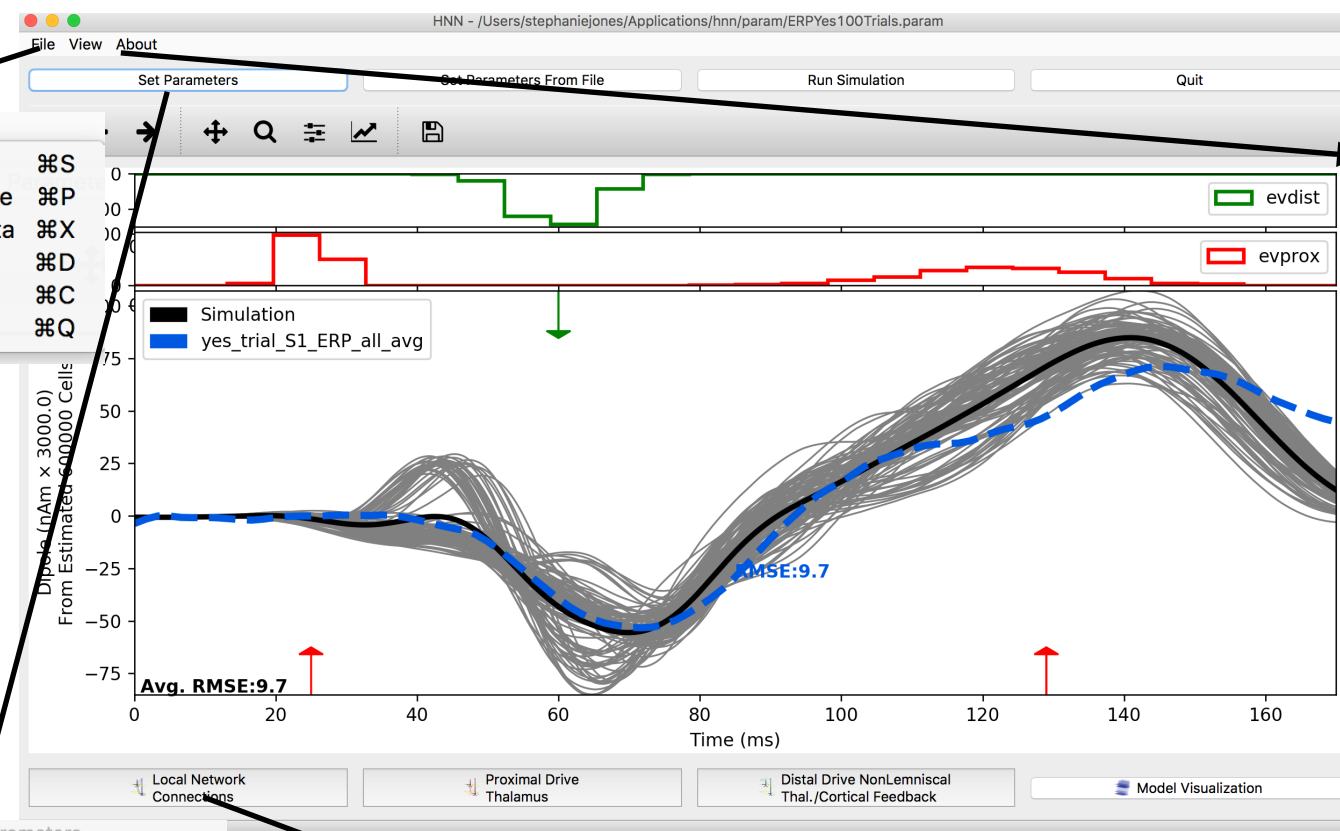
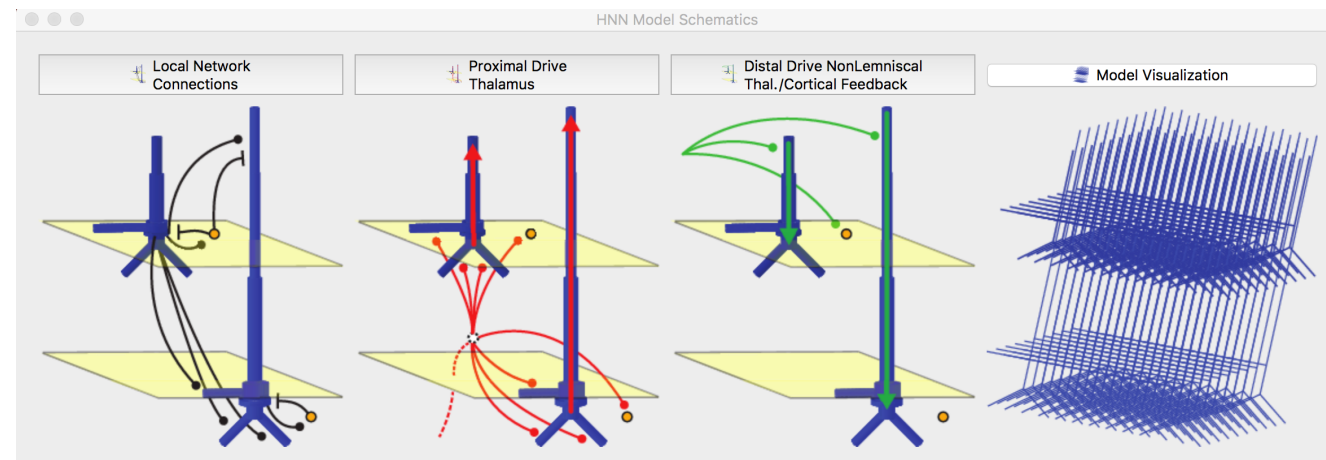
L2/3 Pyr -> L2/3 Pyr NMDA weight (nS) 0.00055125000000

L2/3 Basket -> L2/3 Pyr GABAA weight (nS) 0.05

L2/3 Basket -> L2/3 Pyr GABAB weight (nS) 0.05

Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



File View About

- Run simulation ⌘S
- Set parameter file ⌘P
- Clear canvas/data ⌘X
- Load data file ⌘D
- Clear data file ⌘C
- Exit ⌘Q

View About

- View Simulation Dipoles
- View Simulation Spiking Activity
- View PSD
- View Somatic Voltage
- View Spectrograms

- View Model Schematics
- View Local Network (3D)
- View Simulation Log

- Toggle Average Dipole Drawing
- Change Font Size
- Change Line Width
- Change Marker Size

- Distribute Windows
- Hide Windows ⌘H

Set Parameters

Simulation Name: default

Run Cell

Local Network Synaptic Gains

Rhythmic Proximal Inputs

Rhythmic Distal Inputs

Evoked Inputs

Poisson Inputs

Tonic Inputs

Save Parameters To File

Local Network Parameters

Cells Layer 2/3 Pyr Layer 5 Pyr Layer 2/3 Bas Layer 5 Bas

L2/3 Pyr -> L2/3 Pyr AMPA weight (nS) 0.00110250000000

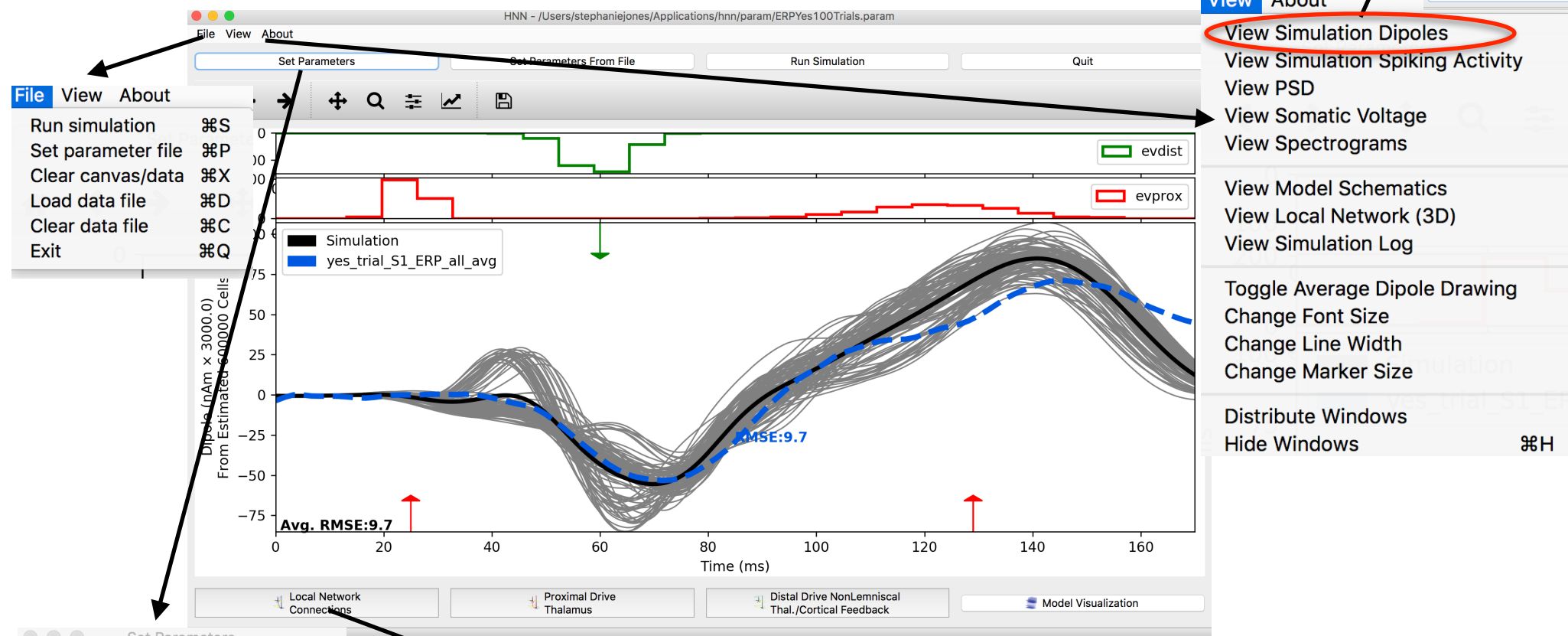
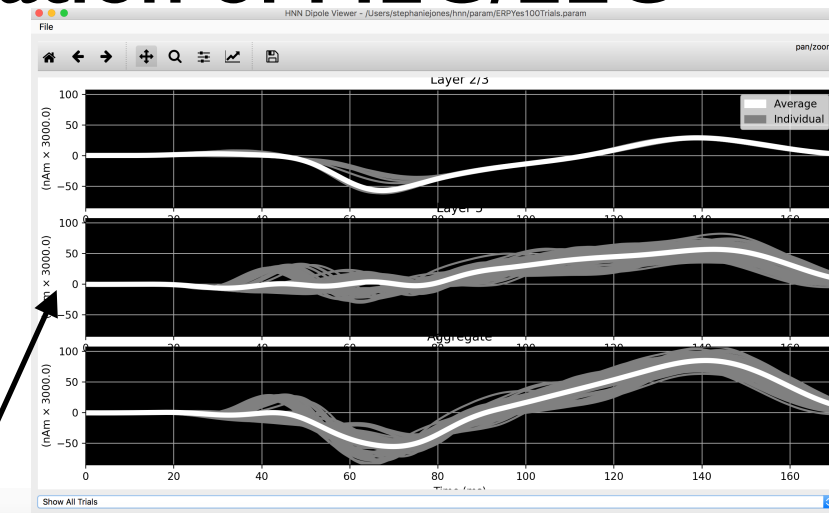
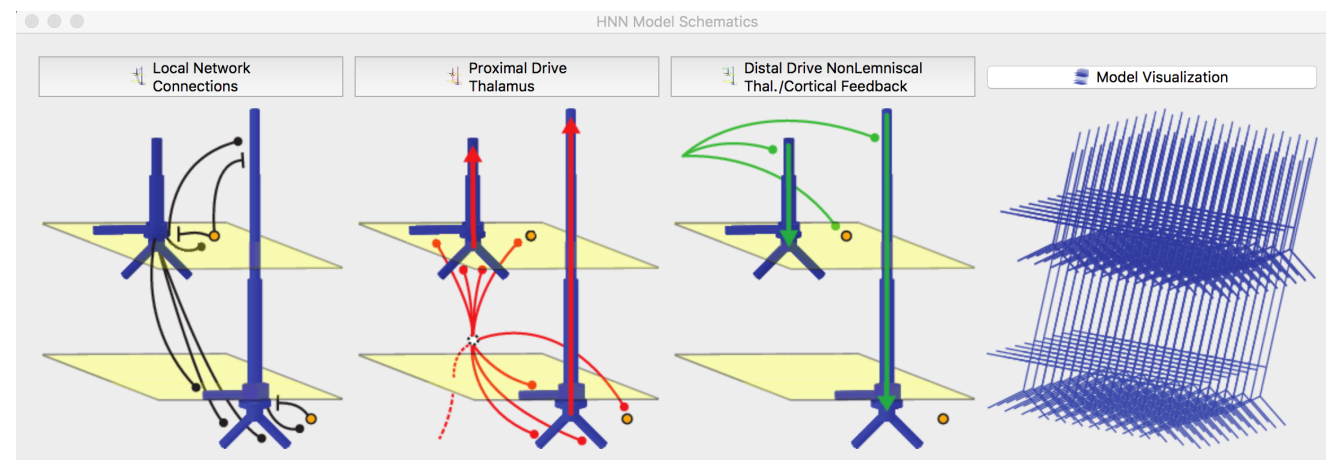
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Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



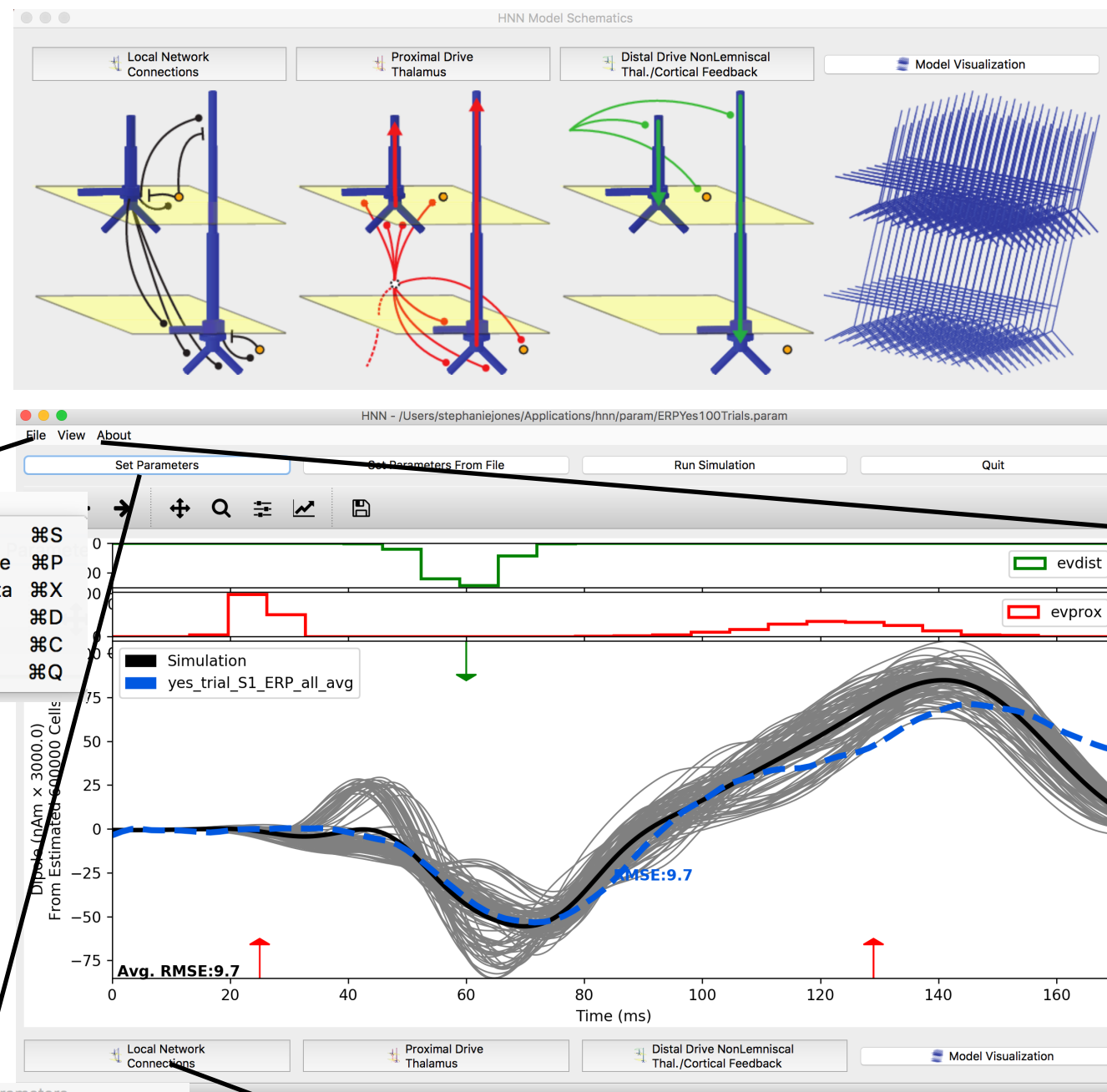
The Set Parameters dialog box allows users to configure the simulation. It includes fields for Simulation Name (default: default) and buttons for Run, Cell, Local Network, and Synaptic Gains. It also has checkboxes for Rhythmic Proximal Inputs, Rhythmic Distal Inputs, Evoked Inputs, Poisson Inputs, and Tonic Inputs, along with a Save Parameters To File button.

The Local Network Parameters dialog box shows the weights for the local network. It includes tabs for Cells, Layer 2/3 Pyr, Layer 5 Pyr, Layer 2/3 Bas, and Layer 5 Bas. The current tab is Layer 2/3 Pyr, showing the following weights:

- L2/3 Pyr -> L2/3 Pyr AMPA weight (nS): 0.00110250000000
- L2/3 Pyr -> L2/3 Pyr NMDA weight (nS): 0.00055125000000
- L2/3 Basket -> L2/3 Pyr GABAA weight (nS): 0.05
- L2/3 Basket -> L2/3 Pyr GABAB weight (nS): 0.05

Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



File View About

Run simulation ⌘S
Set parameter file ⌘P
Clear canvas/data ⌘X
Load data file ⌘D
Clear data file ⌘C
Exit ⌘Q

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⌘H

Set Parameters

Simulation Name: default

Run Cell

Local Network Synaptic Gains

Rhythmic Proximal Inputs

Rhythmic Distal Inputs

Evoked Inputs

Poisson Inputs

Tonic Inputs

Save Parameters To File

Local Network Parameters

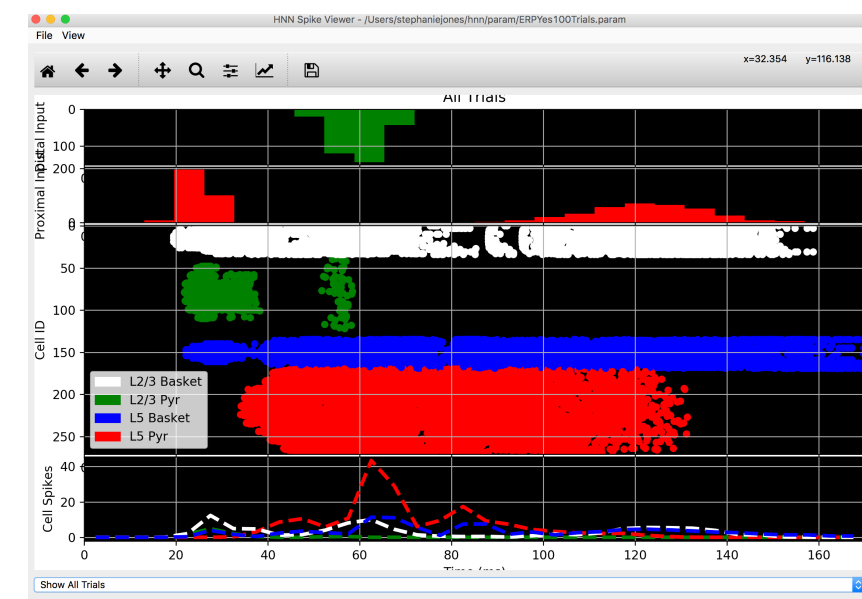
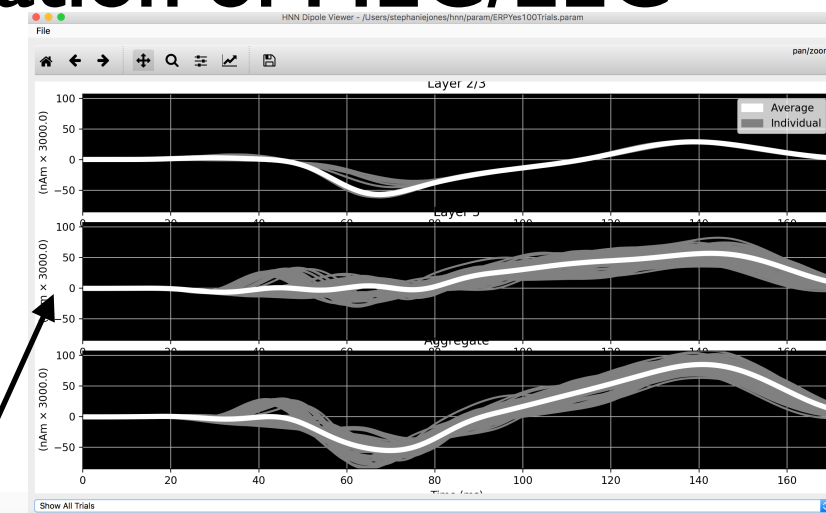
Cells Layer 2/3 Pyr Layer 5 Pyr Layer 2/3 Bas Layer 5 Bas

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L2/3 Pyr -> L2/3 Pyr NMDA weight (nS) 0.00055125000000

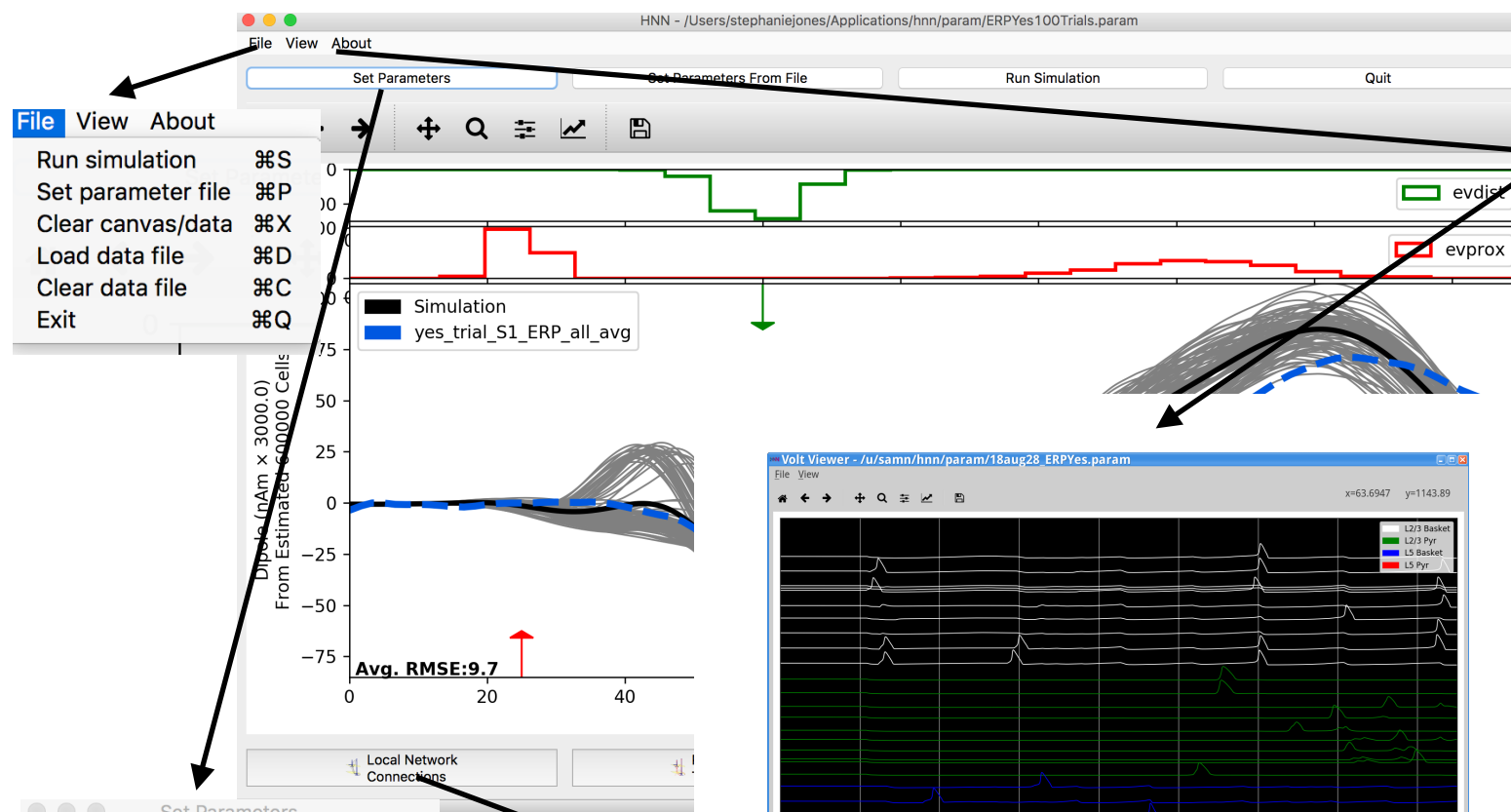
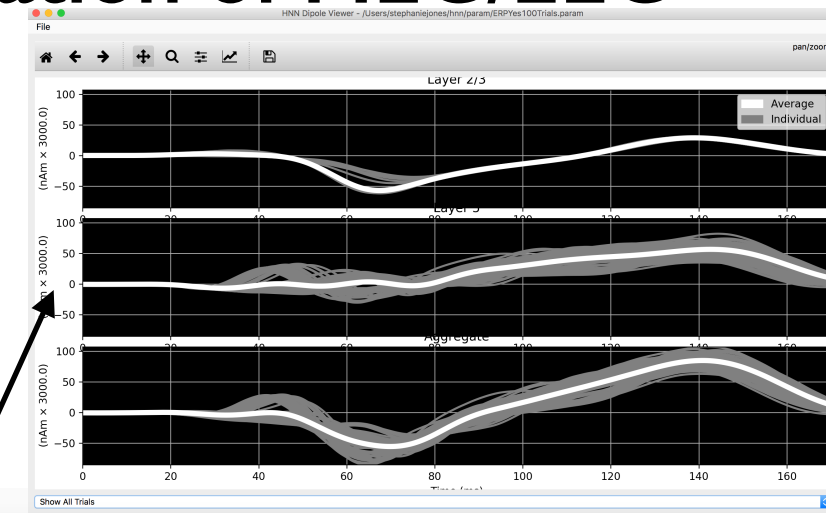
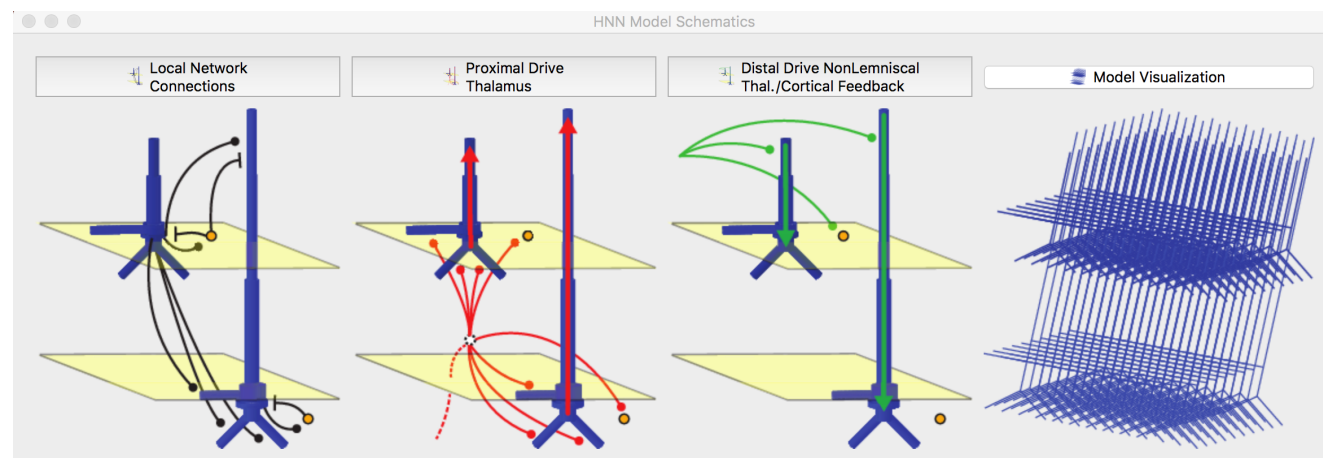
L2/3 Basket -> L2/3 Pyr GABAA weight (nS) 0.05

L2/3 Basket -> L2/3 Pyr GABAB weight (nS) 0.05



Human Neocortical Neurosolver

A new software tool for circuit level interpretation of MEG/EEG



- View Simulation Dipoles
- View Simulation Spiking Activity
- View PSD
- View Somatic Voltage
- View Spectrograms
- View Model Schematics
- View Local Network (3D)
- View Simulation Log
- Toggle Average Dipole Drawing
- Change Font Size
- Change Line Width
- Change Marker Size
- Distribute Windows
- Hide Windows

Set Parameters

Simulation Name: default

Run Cell

Local Network Synaptic Gains

Rhythmic Proximal Inputs

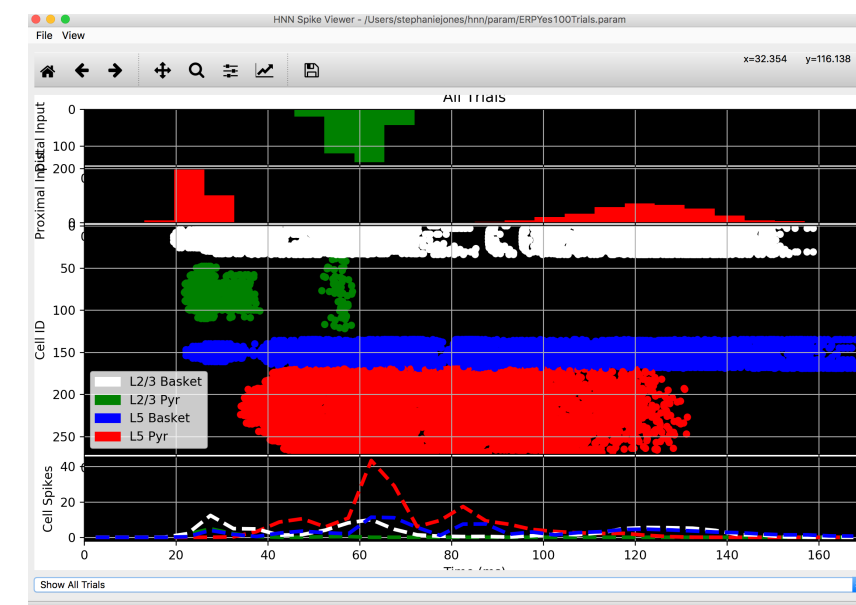
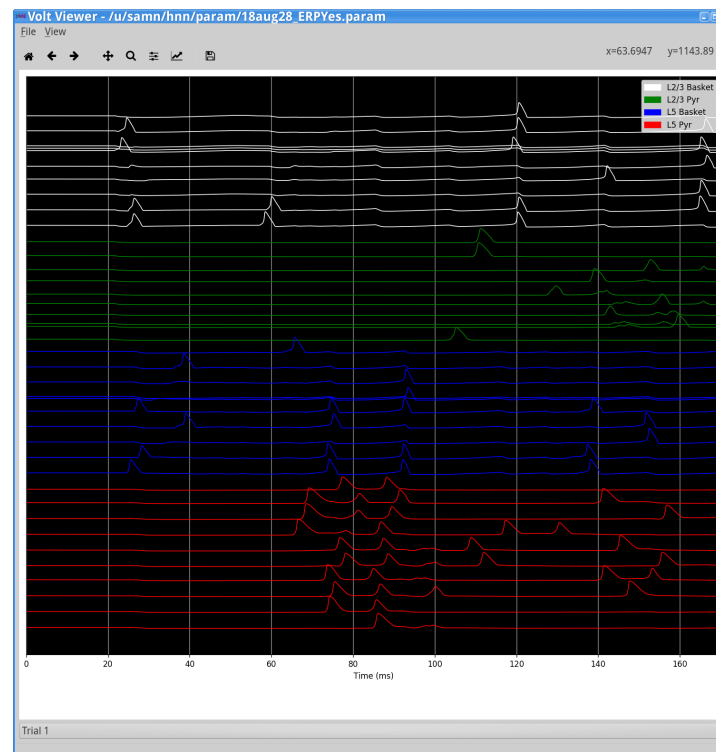
Rhythmic Distal Inputs

Evoked Inputs

Poisson Inputs

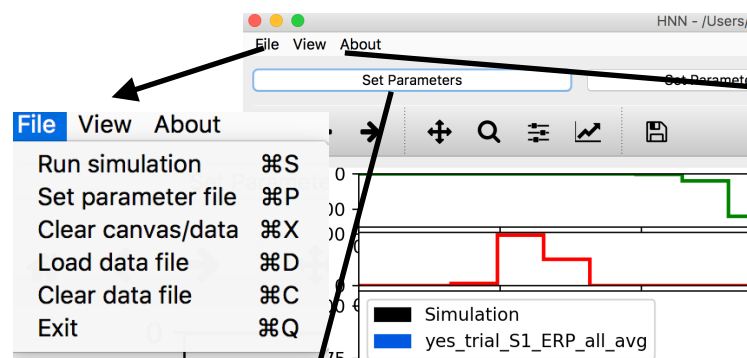
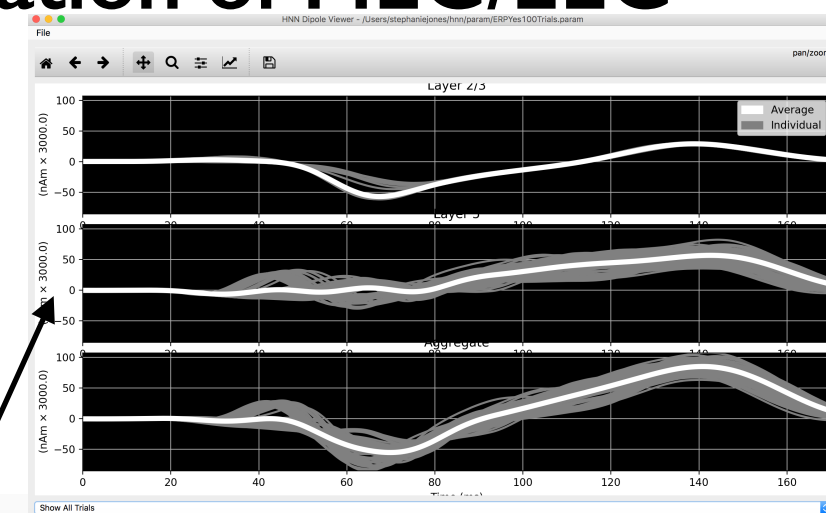
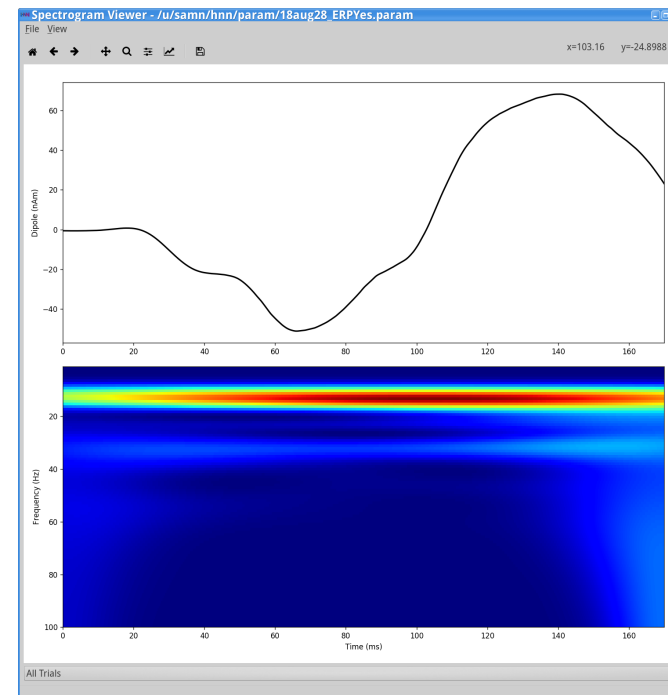
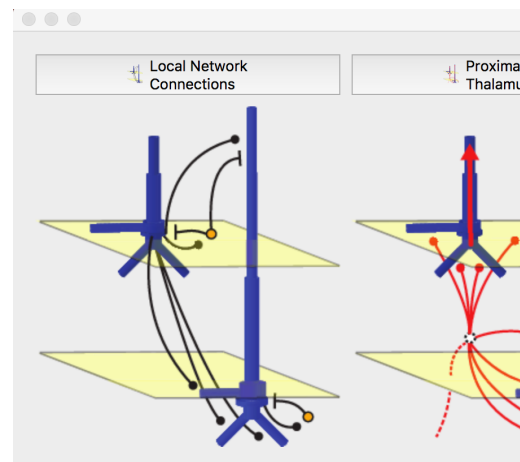
Tonic Inputs

Save Parameters To File

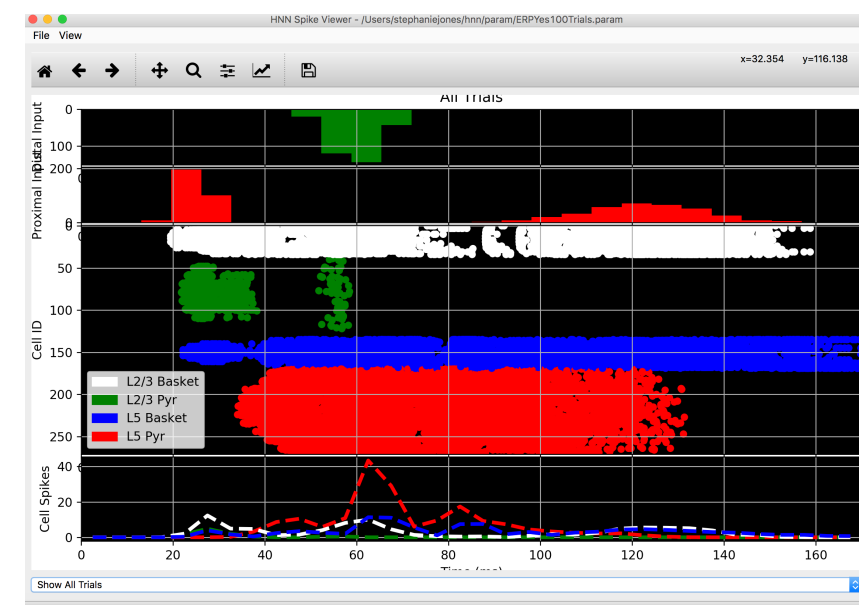
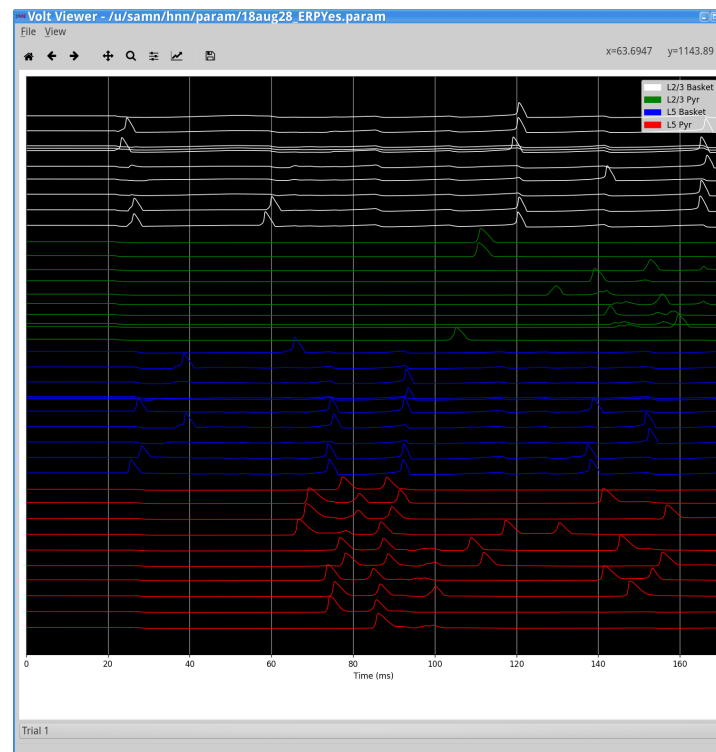
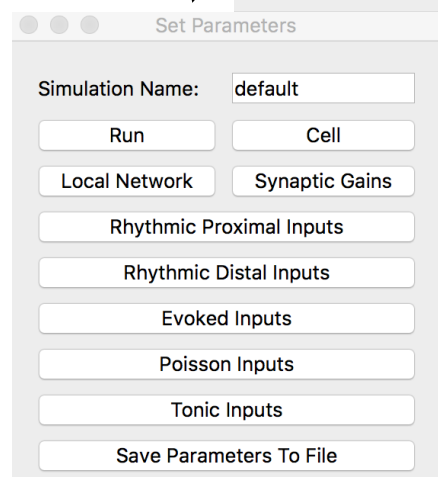


Human Neocortical Neurosolver

A new software tool for the interpretation of MEG/EEG



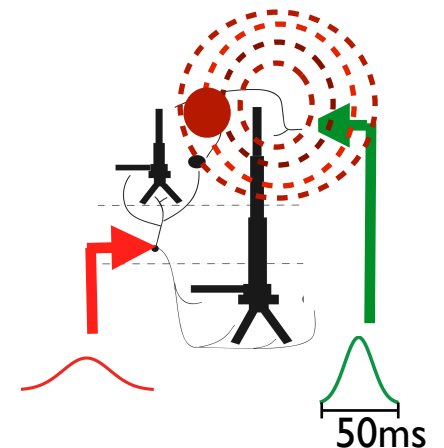
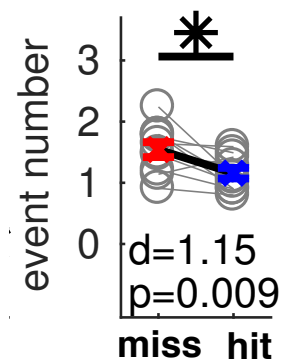
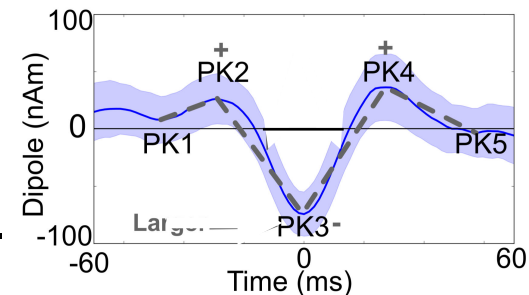
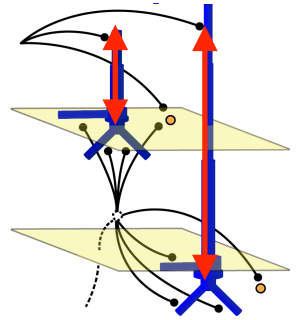
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Conclusions

- HNN is a neocortical column model under thalamocortical / cortico-cortical drive that simulates MEG/EEG primary currents based on their biophysics.
- HNN combined with MEG and invasive animal recordings revealed novel mechanisms and meaning of evoked responses & neocortical beta rhythms.
 - Beta “events” are transient (<150ms) with a stereotypical waveform.
 - The number of beta events (‘rate’) is greater during non-detected / non-attended trials, and non-detected trials have more recent beta events.
 - Beta events emerge from a broad proximal drive simultaneous with a strong distal drive that lasts one beta period ~50ms.
 - Beta decreases the salience of sensory input via recruitment of supra-granular inhibition that decreases the downstream relay of information.
- HNN software can be accessed at <https://hnn.brown.edu>. Please join our google group <https://groups.google.com/forum/#!forum/hnnsolver> and help contribute to turning HNN into a powerful tool for your hypothesis testing needs.



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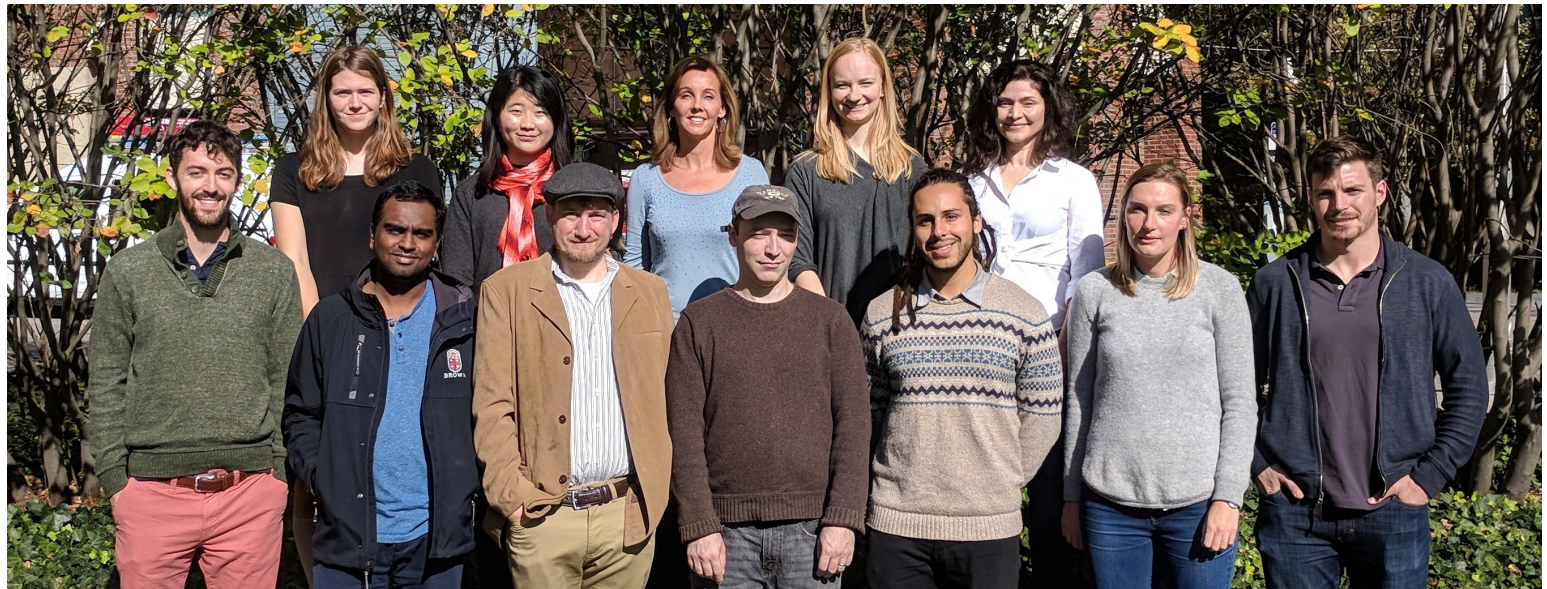
NEURON Team

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HNN development team



Brown Collaborators

mice recordings

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Hyeyoung Shin

human recordings & DBS

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monkey recordings

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Saskia Haegens

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NIMH: *CRCNS* program

Carney Institute for Brain Sciences

Providence VA CfNN



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BROWN UNIVERSITY



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